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THE ASSOCIATION OF INTELLIGENCE WITH MORBIDITY, MORTALITY AND DISABILITY PENSION

EPIDEMIOLOGICAL STUDIES IN A COHORT OF
SWEDISH MEN

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THE ASSOCIATION OF INTELLIGENCE WITH
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- EPIDEMIOLOGICAL STUDIES IN A COHORT OF
SWEDISH MEN

THESIS FOR DOCTORAL DEGREE (Ph.D.)

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What a peculiar privilege has this little agitation of the brain which we call 'thought'
— David Hume

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SAMMANFATTNING

Intelligens uppmätt tidigt i livet har visats ha samband med hälsa senare i livet, men mekanismerna bakom sådana samband är inte helt klarlagda. Det övergripande syftet med avhandlingen var att öka förståelsen för sådana samband, och i synnerhet att undersöka vissa tänkbara mekanismer som skulle kunna förklara dem.

Den svenska värnpliktskohorten 1969-1970 användes i alla fyra studier. Kohorten, som består av 49 321 män födda 1949-1951, kopplades till flera nationella register med information från barndomen upp till 59 års ålder. Exponeringsvariabeln, intelligens, mättes vid värnpliktsmönstring vid 18-20 års ålder. Studierna I-III baserades på hela kohorten. Studie IV baserades på de 2156 män som diagnostiserades med kranskärslssjukdom (CHD) efter 1990. Samband mellan intelligens och de primära utfallen analyserades med överlevnadsanalys (Cox proportional hazards-modeller) eller genom logistisk regression. Information om potentiella förklaringsfaktorer (confounders och mediatorer) hämtades från mönstringsdata, folk- och bostadsräkningen, LOUISE/ LISA-registren och andra nationella register.

Lägre intelligens i tidig vuxenålder var generellt förknippat med sämre utfall. Det inkluderar de flesta indikatorer på hälsotillståndet i tidig vuxenålder (studie III, i tvärsnittsanalyser), självmord och självmordsförsök upp till 57 års ålder (studie I), förtidspension/sjukersättning som beviljats mellan 40 och 59 års ålder (studie II), dödsfall vid första CHD (case-fatality) mellan 40 och 58 års ålder (studie IV) och dödlighet upp till 59 års ålder bland män som överlevde första CHD-tillfället (studie IV). I studierna I och II framkom en gradient över hela intelligensskalan. Inget samband framkom emellertid mellan intelligens och återkommande CHD (studie IV), och vissa diagnoser i tidig vuxenålder hade inget, eller ett positivt, samband med intelligens (studie III). Psykiatriska diagnoser uppvisade det starkaste sambandet med intelligens jämfört med alla somatiska diagnoser och hälsoindikatorer. Sambanden försvagades vid justering för egenskaper och hälsoindikatorer uppmätta i tidig vuxenålder, inklusive personlighetsaspekter, en indikator på sociala problem, riskabelt alkoholbruk och BMI. Dessutom bidrog socioekonomiska och sociala faktorer i vuxen ålder till att försvaga sambanden. Däremot hade socioekonomiska faktorer i barndomen ingen eller ringa påverkan på sambanden i samtliga fyra studier.

Resultaten adderar till, och utökar, tidigare studier av samband mellan intelligens tidigt i livet och hälsoutfall i ett livslöppsperspektiv. Samband mellan intelligens och förtidspension/sjukersättning i sen medelålder samt flertalet diagnoser och hälsoindikatorer i tidig vuxenålder hade inte undersökts tidigare. Av de samvarierande faktorer som ingick i studierna bidrog individuella egenskaper och hälsobeteenden i tidig vuxenålder, och socioekonomiska förhållanden i vuxen ålder, i störst utsträckning till sambanden mellan intelligens och hälsoutfall i denna kohort av svenska män. Även om orsakssamband inte kan fastställas vad gäller förklaringsfaktorena, stämmer resultaten överens med en modell där riskfaktorer kopplade till intelligensnivå ackumuleras över livet. Resultaten tyder också på att intelligens kanske inte har lika stor betydelse när en kronisk sjukdom som CHD redan är etablerad.

ABSTRACT

Intelligence measured early in life is associated with various health outcomes later in life, but the mechanisms underlying the associations are not fully known. The overarching aim of the thesis was to increase the understanding of such associations, and in particular to investigate some potential mechanisms that might explain them.

The Swedish conscription cohort 1969-70 was used in all four studies. This cohort of 49 321 men, born 1949-51, was linked to several nation registers with information spanning from the men's childhood up to age 59. The exposure variable, intelligence, was measured at conscription when the men were 18-20 years old. Studies I-III were based on the full cohort. Study IV was based on a subsample comprising the 2156 men who were diagnosed with coronary heart disease (CHD) after 1990. The associations between intelligence and the primary outcomes were analysed in survival analysis, using Cox proportional hazards model, or by logistic regression. Potential explanatory factors (confounders and mediators) were retracted from conscription, national populations and housing censuses, the LOUISE/LISA registers and other national registers.

In general, lower intelligence in early adulthood was associated with poorer outcomes. This includes most indicators of health status in early adulthood (study III, in cross-sectional analyses), suicide and suicide attempt up to age 57 (study I), disability pension granted between age 40 and 59 (study II), case-fatality in first CHD between age 40 and 58 (study IV) and mortality up to age 59 among the men who survived a first CHD (study IV). In studies I and II, the associations were graded across the intelligence span. However, no association between intelligence and recurrence in CHD was found (study IV), and some diagnoses in early adulthood were not, or positively, associated with intelligence (study III). Psychiatric diagnoses showed the strongest association with intelligence compared to all somatic diagnoses and health indicators. Characteristics and health indicators measured in early adulthood, including personality aspects, an indicator of social problems, substance use and BMI, attenuated the associations in all analyses where such data were introduced. In addition, socioeconomic and social factors in adulthood contributed in attenuating the associations. However, childhood socioeconomic factors had no or minimal impact on the associations.

The results add to, and extend, previous findings of associations between intelligence early in life and health outcomes across the life span. The associations between intelligence and disability pension in late middle age and several diagnoses and health indicators in youth had not been investigated previously. Of the covariates studied, individual characteristics and health behaviours in youth, and socioeconomic circumstances in adulthood, were the most important contributors to the associations in this male cohort. Although causality cannot be determined, the findings are compatible with the notion of an accumulation of risks associated with intelligence across the life course. The findings also suggest that intelligence might not be as important when a chronic disease such as CHD is already established.

LIST OF PUBLICATIONS

This thesis is based on the following publications, referred to in the thesis by their Roman numbers. The published papers are reprinted with kind permission from Cambridge University Press and Elsevier, or available by open access.

- I. Sörberg, A., Allebeck, P., Melin, B., Gunnell, D., & Hemmingsson, T. (2013). Cognitive ability in early adulthood is associated with later suicide and suicide attempt: the role of risk factors over the life course. *Psychological medicine*, 43(01), 49-60.
- II. Sörberg, A., Lundin, A., Allebeck, P., Melin, B., Falkstedt, D., & Hemmingsson, T. (2013). Cognitive ability in late adolescence and disability pension in middle age: follow-up of a national cohort of Swedish males. *PloS one*, 8(10), e78268.
- III. Sörberg, A., Allebeck, P., & Hemmingsson, T. (2014). IQ and somatic health in late adolescence. *Intelligence*, 44, 155-162.
- IV. Sörberg Wallin, A., Falkstedt, D., Allebeck, P., Melin, B., Janszky, I. & Hemmingsson, T. (2014). Does high intelligence improve prognosis? Associations of intelligence with recurrence and mortality among Swedish men with coronary heart disease. *The Journal of Epidemiology and Community Health*, e-pub ahead of print: doi:10.1136/jech-2014-204958

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LIST OF ABBREVIATIONS AND CONCEPTS USED

BMI	Body Mass Index
BP	Blood Pressure
CHD	Coronary Heart Disease
CI	Confidence Interval
CVD	Cardiovascular Disease
ESR	Erythrocyte Sedimentation Rate
<i>g</i>	General Factor of Intelligence, <i>g</i> -Factor
HPA	Hypothalamic–Pituitary–Adrenal Axis
HR	Hazard Ratio
ICD	International Classification of Diseases
IQ	Intelligence Quotient
LISA	The Longitudinal Integration Database for Health Insurance and Labour Market Studies
LOUISE	The Longitudinal Database of Education, Income and Employment
MI	Myocardial Infarction
NYK	Nordic Occupation Classification (in Swedish: Nordisk Yrkesklassificering)
OR	Odds Ratio
SEP	Socioeconomic Position
SRH	Self-Rated Health
Stanine	Standard-Nine
Intelligence	A general capacity for reasoning, problem solving, abstract thinking, comprehending complex ideas and learning from experience.
Cognitive ability	A wider concept that can be used synonymously with intelligence, but can also refer to specific abilities that correlate with general intelligence to various degrees. Intelligence tests often consist of a battery of tests of different abilities.
IQ	Intelligence as expressed in intelligence tests.

1 BACKGROUND

1.1 A BRIEF INTRODUCTION TO COGNITIVE EPIDEMIOLOGY

The association between intelligence and health has been increasingly investigated during the last 15 years, since Whalley and Deary presented their findings that intelligence measured at age 8 predicted mortality up to age 76 in a cohort of Scottish men and women [1]. The term “cognitive epidemiology” was introduced in 2004 [2], in the meaning of studies of associations between pre-morbid intelligence and morbidity and mortality, and what was perhaps first regarded with some skepticism is now well established: higher intelligence is associated with less somatic and psychiatric morbidity and longer lives, with few exceptions [3,4,5].

Already in 1990, O’Toole found that men scoring lower on the army intelligence test at enlistment had a higher risk of dying in a motor vehicle accident after military service compared with higher scoring men [6]. Soon after came the findings that intelligence also predicted all-cause mortality after military service, up to early midlife [7]. Still, it was not until Whalley and Deary published their study in 2001 that the new research area bricked up, and their study was followed by many more. Holding a biopsychosocial perspective, that is, the notion that biological, psychological and social processes interact in morbidity processes [8], the research area can be placed in the field of social epidemiology.

The association of intelligence with morbidity and mortality has now been confirmed in many longitudinal studies using different cohorts, predominantly from Scandinavian and English-speaking industrialized countries. Table 1 shows some of the cohorts used, and examples of their findings. Several of the cohorts contain a large number of people, yielding quite reliable data. The measures of intelligence vary between cohorts, also contributing to the robustness of the associations, and are in some cases validated against established intelligence quotient (IQ) tests [3,9,10,11,12,13,14]. A gradient is often reported, such that the associations are nearly linear across the range of intelligence [10,15,16,17,18,19,20,21,22]. An example is the risk for all-cause and injury mortality in a study of the Swedish conscription cohort 1969-70 [15], shown in Figure 1. In this study, the risk for mortality up to age about 50 was almost 50% higher among men with an average intelligence score (5), and around 150% higher among men with the lowest score (1), compared to men with the highest score (9).

The magnitudes of the associations are often on par with other well-known risk factors for public health. For example, in a cohort of male Vietnam veterans who had their intelligence assessed at recruitment, in analyses of relative index of inequality (RRI), intelligence was a stronger predictor for all-cause mortality up to year 2000 than blood pressure, cholesterol levels and BMI measured in middle age; and not very far behind smoking [23]. For an illustration of what the association means in terms of life expectancy, Kajantie et al [24], using the male Helsinki birth cohort, calculated that the mortality differences between the highest and lowest quartile of ability corresponded to around three years lost in the lowest group.

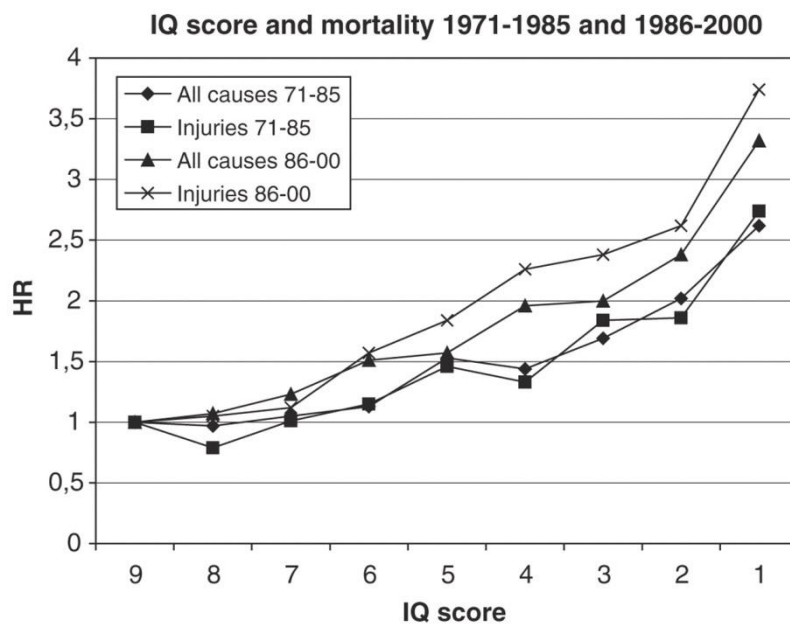


Figure 1. The risk of mortality increases across the IQ range, from highest to lowest, among men in the Swedish conscription cohort 1969-70 [15]. Mortality from injuries and all causes from about 20 to 50 years of age, divided into two time periods, is shown. Reprinted with permission from Oxford University Press.

As the associations between intelligence and mortality were increasingly researched and confirmed in several studies, more ways to investigate the possible underlying mechanisms were explored. When the attention is turned to the mechanisms, all-cause mortality is a quite crude outcome since the mechanisms probably differ between causes of death. In addition, morbidity and other health-related outcomes are important matters in their own right. Hence, specific causes of death, various types of morbidity and health indicators, and also established risk factors such as smoking [25,26,27,28,29,30,31] and diet [32,33] have been studied in relation to pre-morbid intelligence. For example, lower intelligence in youth is found to be associated with cardiovascular morbidity and mortality in many studies, including the Scottish Mental Survey 1932 [34], the Danish Metropolit cohort [35], and the Swedish conscription cohort of one million men [36,37]; suicide in Scandinavian male cohorts [20,38,39] (but in the Swedish UGU-cohort, an association of intelligence with suicide was only found among men, not women [40]), and alcohol-related mortality in the Swedish conscription cohort 1969-70 [41]. On the other hand, cancer morbidity and mortality is not consistently associated with intelligence [15,42,43,44].

Other health conditions and indicators that have been found to be associated with lower intelligence include atherosclerosis [45,46], the metabolic syndrome [47,48], unintentional injuries [9,49,50], constraints in activities of daily living in middle age [51] and old age [52], inflammation [53,54] and reduced lung function [27,55]. However, no association was found between intelligence and self-reported symptoms of poor health in a sample of working women and men in Sweden [56].

Table 1. Examples of cohorts used in studies of intelligence early in life and health outcomes later in life.

Cohort	Participants	Test of intelligence	Examples of findings
Scottish mental surveys 1932 and 1947	All Scottish children born in 1921 and 1936, tested for IQ at age 11; linkage to data later in life determines study samples, for example Aberdeen study N≈2800, men and women.	Moray House Test No 12; 71 items measuring general, spatial, and numerical reasoning.	The lowest quartile of IQ was associated with mortality up to age 65, but not in an older age span [1].
British birth cohorts 1946, 1958 and 1970	British men and women born during a single week in their birth year, tested for IQ at age 8, 11 and 10, respectively. N≈ 2 900-15 000	Different tests of general ability, all including verbal and non-verbal components.	Lower IQ was associated with psychological distress (the Malaise inventory) at age 30/33 in a study including the 1958 and 1970 cohorts [57].
Danish Metropolit 1953	Danish men, tested for IQ at age 12, and most also at conscription at age 18. N≈11 500	Härnqvists intelligence test at age 12: verbal, spatial and inductive tests; Børge Priens Prøve at age 18: letter matrices, verbal analogies, number series, and geometric figures.	Lower IQ in childhood and early adulthood had graded associations with fatal and non-fatal injuries up to age 48 [9].
Swedish conscription cohort 1969-70 and 1969-94	Swedish men in mandatory conscription for military service at age 18-20. N≈49 000 (1969-70); ≈1 100 000 (1969-94)	Military tests of general ability, four parts: logic/inductive, verbal and visuospatial ability, and technical comprehension.	In the larger cohort, lower IQ was associated with an increased risk of hospitalizations with psychiatric diagnoses, including schizophrenia, mood disorders and personality disorders [21].
The Vietnam Experience Study	Men entering US army service 1965-71. N≈18 000	The Army General Technical Test; verbal and arithmetic reasoning.	Lower IQ was associated with systematic inflammation (the erythrocyte sedimentation rate, ESR) at age about 38 [54].
The 1979 US National Longitudinal Study of Youth	US adolescents, male and female, tested for IQ at age 16-23. N≈12 000.	The Armed Forces Qualification test: arithmetic reasoning, word knowledge, section comprehension, mathematics knowledge.	Of a range of self-reported disorders and conditions at age 40, higher IQ was associated with a lower risk of many of them, but higher risk of a few of the disorders [58].

Lower intelligence is also associated with psychiatric disorders [12,21,59,60,61,62,63]. For example, lower intelligence in early adulthood predicted various psychiatric diagnoses from hospital records in Swedish and Danish men [21,61,62], psychiatric diagnoses by diagnostic interview in the Vietnam Experience Study [12], and personality disorders in a Swedish cohort of women and men born in 1953 in Stockholm [19], although the risk for bipolar disorder might be slightly elevated also among those with high intelligence [64]. Furthermore, psychological symptoms are also associated with lower intelligence [57,59,65,66,67,68]. For example, in the British 1958 and 1970 cohorts, lower childhood intelligence was associated with psychological distress at age 33 [57]; in the British 1946 cohort higher childhood intelligence was associated with fewer symptoms of anxiety and depression but only in women, not men [67]; and in a birth cohorts of girls and boys in New Zealand lower childhood intelligence was associated with anxiety in adolescence [68]. However, in a British birth cohort lower intelligence at age 8 was associated with a lower risk for non-suicidal self-harm at age 12 in girls and boys at age (that is, the opposite direction compared to most other associations)[69].

Still, the vast majority of findings point to the fact that intelligence level, measured early in life, is indeed predictive of important health outcomes. However, the mechanisms underlying these associations are still not fully understood. In order to get an idea of how intelligence can be predictive of illness and death across the life span, it is perhaps first necessary to depict what we mean by intelligence.

1.2 WHAT IS INTELLIGENCE?

It is sometimes argued that intelligence tests measure simply test-taking skills, and that it has little validity over and above the test situation, as exemplified by Borings notion: "intelligence is what the [intelligence] tests test" [70, p. 35](although it is worth mentioning that Boring himself elaborated after this statement that IQ indeed matters for important life outcomes). The finding that tests of general cognitive ability predicted illness and early death mitigated this assumption. Although cognitive epidemiology is a quite new research area, it was already in 1992 that O'Toole and Stankov argued that their finding of an association between general intelligence and mortality in middle age provided the "ultimate validity of psychological tests" [7].

1.2.1 Intelligence, cognitive ability and IQ

The basis of this thesis is the research using cognitive tests that are designed, or similar to tests designed, to measure IQ. The terms intelligence and cognitive ability are in some regards used interchangeably, depending on the context. More specifically, intelligence is regarded more as an overarching ability, with many aspects of cognitive ability as correlated traits, in accordance with the concept of *g* described below. IQ denotes the expression of intelligence in tests of general intelligence.

1.2.2 Models of intelligence

Psychometric intelligence and hierarchical structures

It was already in the end of the 19th century that IQ tests were invented, as a means of predicting educational success in children [71]. Since then, IQ tests and similar tests of cognitive ability have been further developed and are now used in various fields, but the basic assumption remains that they capture some general ability that is highly predictive of performance over long time spans. This general ability is sometimes labeled the *g*-factor, or simply *g* [71,72]. There is considerable support for *g* as an underlying factor in cognitive performance [73,74], that it is highly heritable [73,75], and generally quite stable across life [76,77]. Neurobiological research has suggested that *g* might be determined by the overall efficiency of the brain's networking, rather than some specific areas of the brain [78].

In an attempt to mitigate criticism of the notion of *g* as an important factor for people in general during the mid-90's, Gottfredson wrote a definition of general intelligence and had it accredited by 51 other professionals. It holds that "Intelligence is a very general capability that, among other things, involves the ability to reason, plan, solve problems, think abstractly, comprehend complex ideas, learn quickly and learn from experience. It is not merely book learning, a narrow academic skill, or test-taking smarts. Rather, it reflects a broader and deeper capability for comprehending our surroundings — 'catching on', 'making sense' of things, or 'figuring out' what to do. Intelligence, so defined, can be measured, and intelligence tests measure it well" [79, p. 13]. This view of intelligence is commonly used in research on individual differences in intelligence, including cognitive epidemiology.

In contemporary psychometric models of intelligence, there is often a hierarchical structure with a set of abilities in a few sets of strata loading on *g* as a latent factor of intelligence [80]. The structures vary according to the model in question. One common model describes the two broad categories of fluid and crystallized intelligence, the former denoting on-the-go problem solving and efficient processing and the latter consolidated knowledge and skills (similar to the performance and verbal scales, respectively, in the commonly used Wechsler battery of neuropsychological assessment [81]). Other models can include more dimensions, for example the three-stratum theory in which several abilities load onto eight broader categories, in turn loading on *g* [80].

Non-psychometric models of intelligence

Emotional intelligence is a construct that, in short, denotes the ability to understand and regulate emotions, and is often measured by self-reports or others' evaluations of behaviour [82]. The exact nature of emotional intelligence and how it should be measured is however debated, and criticism has been raised of its validity [82,83]. Some argue that emotional intelligence is related to general intelligence and can be thought of as an ability that enhances thinking [82], while others see it more as a personality measure unrelated to intelligence [84]. Emotional intelligence is widely used in popular science and in measures of employability, but its use in predicting work

performance and other outcomes over and above established measures of intelligence and personality is disputed [83,85].

Some models discard the idea of g . One of the most well-known is Gardners “Multiple intelligences”, holding that there are at least eight distinct types of intelligences that are related to creative production or problem solving, for example logical-mathematical, interpersonal, and bodily-kinesthetic intelligence [86]. This model is popular in educational settings, with good results on effort, motivation and learning [80]. It is, however, not as useful in contemporary research on individual differences in intelligence, partly because of a lack of scientific evidence of uncorrelated abilities independent from g [5].

1.2.3 Individual differences in intelligence

In general populations, there are variations in intelligence. These variations tend to follow a normal distribution such that most people are within the average level of intelligence while fewer are closer to the extremes of higher or lower intelligence, much like other traits such as height.

Several different factors contribute in determining an individual’s intelligence level. The genetic contribution to the individual level of intelligence is quite strong, and is found to increase with age from about .20 in early childhood to possibly .80 in late adulthood [87]. This increase is proposed to happen because of the increasing agency and possibility to shape one’s environment according to one’s genetic constitution with increasing age, while the environment you are presented with might affect you more at a young age [87,88]. Moreover, the genetic contribution to the expression of intelligence (phenotypic intelligence) is found to be higher in higher socioeconomic strata [89,90], possibly because a more affluent environment supports the maximization of cognitive development and hence increase the genetically based differences [91].

Since genetics is not the only determinant of intelligence, environmental factors are clearly also contributing. Early life factors that might affect cognitive development and intelligence are sought in various areas. Exposure to lead [92], pre- and postnatal nutrition [93], failure to thrive (gain weight) during the first week after birth [94], and birth order [95] are some examples of factors that are found to be associated with cognitive development. For some factors, the causal effect of environmental exposure is difficult to disentangle from the genetic effect. For example, the association of breast feeding with higher IQ in children might be explained by mothers with higher intelligence being more likely to breast feed their infants, who in turn are more likely to have inherited their mothers’ higher intelligence, but findings are ambiguous [96,97,98].

Adverse events during upbringing, such as having a mentally ill parent or experiencing sexual or physical abuse, have been found to predict lower intelligence [99,100,101]. However, few studies have been able to disentangle the effect of parental intelligence which is correlated with childrens’ intelligence. For example, children of parents with lower intelligence have been shown to have higher risks for injuries and sedentary

behaviours [102,103], indicating that children's well-being is affected by parental intelligence level. In a study of 800 US adolescents, those with higher intelligence reported less exposure to trauma during upbringing [104]. Thus, some of the association between adversity and lower intelligence might be due to differences in exposure according to intelligence level. On the other hand, given experienced adversities, children and adolescents with higher intelligence seem to be more resilient and show less behavioural problems in their late teens [105,106,107], so the association might run both ways (possibly putting youths with lower intelligence in an even more vulnerable position).

It has been suggested that intelligence is raised by education [108,109]. However, few have been able to disentangle the actual effect of education from the tendency of people with higher intelligence to perform better and stay longer in school, but studies attempting to control for this tendency show that one year of schooling is associated with a raise of around 2 or 3 IQ points (on the traditional Stanford-Binet scale with a mean of 100 and standard deviation of 15) [110,111,112,113]. Other suggested ways to raise intelligence are cognitive training [114], and early educational interventions and interactive reading in childhood [115], which have been found to enhance cognitive skills in some studies. There is also some evidence that physical exercise can raise cognitive ability in youth [116,117] as well as later in life [118], possibly by neurobiological mechanisms [117,119].

However, there are concerns whether a raise in IQ test performance after an intervention corresponds with real-life outcomes such as mortality, or if such a raise mostly reflect better test-taking skills or specific cognitive skills [109,120]. Meghir et al [110] found that although more schooling during a reform in Sweden appeared to raise intelligence, as measured at conscription, more schooling had no effect on mortality at age 40 to 60. On the other hand, Lager et al found that the association between more schooling and lower mortality was partly explained by raised intelligence, also measured at conscription [121]. In combined samples from school reforms in various European countries, more schooling increased delayed memory at age about 60, but had no effects on fluency, numeracy, or orientation-to-date [122].

1.3 HOW IS INTELLIGENCE LINKED TO HEALTH AND EARLY DEATH?

As mentioned in section 1.1, numerous studies have shown that lower intelligence is associated with illness and death. The mechanisms underlying these associations are not yet fully understood, but several hypotheses have emerged during the development of this research area. Since the first studies concerned mortality, the first hypotheses were targeted on this specific outcome. As more outcomes have been found to be predicted by intelligence, including psychiatric illness and reduced work ability, some completing hypotheses to explain them have emerged. But let us start with four hypotheses that contributed to the foundation of cognitive epidemiology as a research area, and still keep coming up in the literature in different versions.

1.3.1 Four hypotheses

Whalley and Deary conducted the first study using population-based data with IQ measured in childhood and follow-up into old age, showing that intelligence predicted mortality [1]. They suggested four potential mechanisms that might underlie this association, which have been somewhat modified over the years [4,123]:

1. Bodily insults early in life, related to lower health standards in poorer households, might affect the cognitive development as well as the risk for later illness and death. However, later findings have shown that socioeconomic factors in childhood typically have little explanatory effect on the association between intelligence and mortality. In a meta-analysis including 16 longitudinal studies, childhood socioeconomic position did not attenuate the association between intelligence and mortality much [3], indicating that it is not an important mechanism in the association. However, other circumstances early in life might also affect cognitive development as well as later health, such as psychosocial environment. For example, in the British 1958 cohort, adjusting for parents' interest in the child's education attenuated the association between childhood intelligence and mortality up to middle age, while adjusting for the occupational class of the father had minimal effect on the association [10].
2. Bodily system integrity, or a more "well-wired" body [124], might increase the efficiency of the brain, thereby enhancing IQ test performance, and also produce a somatically more healthy system. Findings that reaction time explained much of the intelligence-mortality association in a Scottish cohort with a measure of intelligence in mid-life supports this hypothesis [125]. On the other hand, findings pointing to more contextually dependent associations, for example associations that differ between men and women, might speak against this hypothesis [126] (although findings of variants in the associations does not eliminate the possibility that some of the intelligence-health associations might be at least partly explained by physiological composition).
3. People with higher intelligence tend to end up in more advantageous positions as adults, because they tend to attain more education, better job positions and safer environments, which in turn are associated with better health. This mechanism is supported by findings that socioeconomic factors in adulthood, such as educational attainment, occupation and income explain some, and sometimes all, of the associations between intelligence and health outcomes [3,127,128]. Education tend to have the strongest attenuating effect on the associations, which should be interpreted with caution since education might be a proxy for intelligence, and adjusting for education might be regarded as an overadjustment [129].
4. Higher intelligence might be helpful in making healthy choices, and manage one's disease in case of sickness. An association between health literacy, a skill encompassing the ability to understand health information and make appropriate health decisions which is closely related to general cognitive abilities [130], and predicts mortality [131], has been put forward as support for

this hypothesis [132]. The hypothesis is further supported by findings in various populations that people with higher intelligence are more likely to eat more healthy [33], abstain from or quit smoking [25,26,27,28,29,30,31] and have lower BMI [133,134]. However, there are contradictory findings; in a cohort of Swedish women, there was no association between intelligence and a number of health-promoting behaviours [135]; and findings on alcohol are ambiguous [41,136,137].

An illustration of the relations of these four groups of factors with intelligence and morbidity and mortality is depicted in Figure 2. Note that they are not regarded as mutually exclusive, but might all contribute in various proportions. Early life factors and system integrity are suggested to affect both intelligence and the outcomes, and can therefore be regarded as confounding factors; adult position and health behaviours might instead act as mediators, in the sense that a person at any level of intelligence would have the same risk as a person at another level, given that they shared the same socioeconomic and social circumstances, and had the same health behaviours (disregarding the other possible mechanisms).

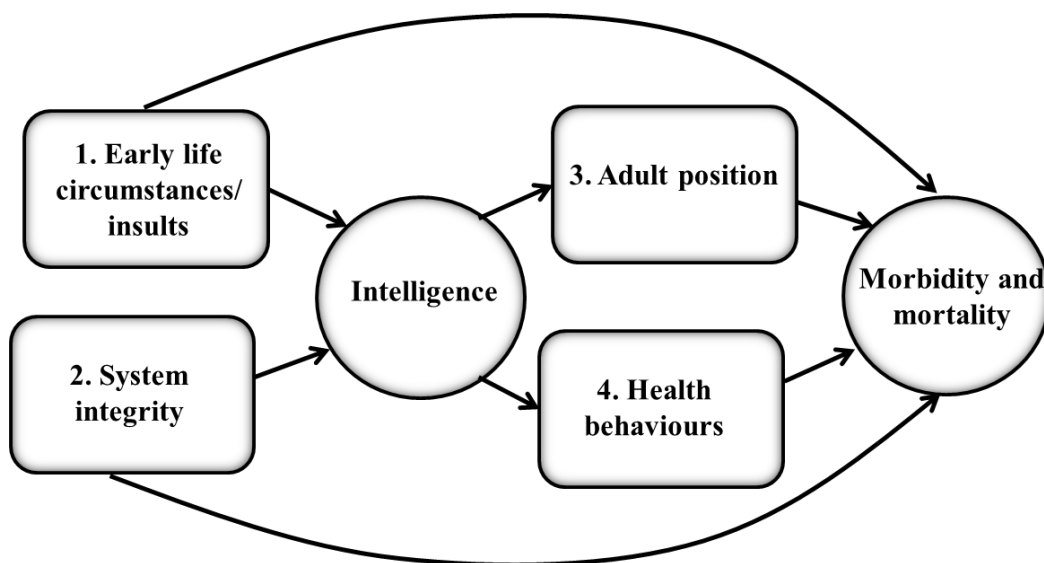


Figure 2. Conceptual model of the four hypothetical mechanisms underlying the association of intelligence with morbidity and mortality, originally presented by Whalley & Deary 2001 [1].

1.3.2 Other possible mechanisms

In 2007, a more complex model was presented in a review article on intelligence and mortality [123, p. 284]. This model also included the role of psychiatric illness. Earlier studies had linked intelligence to psychiatric illness [138,139], but more recently in large cohorts that were also used in studies of intelligence and mortality [12,21,61,64]. However, the role of psychiatric illness has not been much investigated as an

explanatory factor in the intelligence-mortality association. Neither has early psychosocial circumstances and childhood adversities, despite that they have been found to be associated with cognitive ability. There is evidence for negative effects of adverse circumstances on cognitive functions and the possible neurophysiological mechanism for these effects [101], and negative effects on both somatic and psychiatric health is also established [140,141]. This makes psychosocial circumstances and psychological distress potential confounders in the association of intelligence with morbidity and mortality, in addition to psychiatric illness.

A related factor is personality. The personality aspects emotional stability and dependability have been found to interact with intelligence, such that people with low stability or dependability in addition to low intelligence had particularly increased mortality in longitudinal studies [13,142]. However, few have studied the role of personality as an explanatory factor in the associations of intelligence with health outcomes. There have been attempts to study associations between personality and intelligence [143], as well as personality and morbidity and mortality [144]. Since there is at least some evidence of such associations, personality might also be a confounder or mediator.

It should be noted that other mechanisms are suggested to underlie correlations between average intelligence and health on a national level, for example by prevalence of infectious diseases hampering cognitive development [145], environmental challenges evolutionarily shaping differences in intelligence [146], or differences in educational policies and other socioeconomic and political circumstances [147]. Others emphasize that intelligence measures are poorly adapted to non-Western cultures and developing countries which might produce misleading results [148]. Any further elaboration on the matter is however beyond the scope of this thesis. The main studies in cognitive epidemiology are, so far, primarily based on data gathered in industrialized societies, mainly in the UK, US and Scandinavia, and are conducted at the individual level. Some, including the Scandinavian conscript cohorts, are quite homogenous with regards to culture and ethnicity. Therefore, differences between countries and cultures are not problematic within these studies; but generalizability beyond Western, high-income countries and cultures is limited.

1.3.3 Areas for further study

Suicide and suicide attempt

Suicide is a major cause of death, not least among young men [149]. Suicide and suicide attempt are associated with lower intelligence [15,17,20,38,39,40,68,150], but the mechanisms are unclear. Previous studies have found that - in line with associations of intelligence with all-cause mortality - childhood socioeconomic position did not seem to explain the associations of intelligence with suicide [15,20,38,40] and suicide attempt [17,38] while socioeconomic position in adulthood partly attenuated the association with suicide [15]. It is possible that lower socioeconomic position and social status leads to poorer mental health [151], thereby contributing to this effect. However, in the Danish Metropolit cohort, adjusting for mental illness at conscription attenuated the associations of intelligence with suicide and suicide attempt [38],

indicating that poor mental health emerging already in early adulthood contribute to the associations.

In addition to the hypotheses depicted in Figure 2, there are some additional hypotheses regarding the mechanisms underlying the association of intelligence with suicidal behaviour, and with mental disorders which is a related outcome and a risk factor for suicidal behaviour [149]. For example, there might be a shared etiology for intelligence and mental disorders, such as common genetic bases, which might confound the association [12,60]. The latter explanation also includes the idea of bodily system integrity, explained in section 1.3.1, possibly through the hypothalamic–pituitary–adrenal (HPA) axis, the growth hormone axis, and other systems [67] which influence mental health and cognitive function [152,153]. Adverse experiences early in life, for example separation from parents, neglect and abuse [153], might also affect these systems and therefore underlie the association [17,67]. Further, a lower ability to solve problems in daily life and to cope with stressful events, that might come with lower intelligence [154], has been proposed to increase psychological stress and vulnerability to mental disorders [60,67]. A related construct, emotional intelligence - often defined as the ability to understand and manage emotions (also mentioned in section 1.2.2) - might also be associated with general intelligence and with suicidal behaviour [155] and thereby account for some of the association [17].

Thus, many variables originating early in life might be interrelated and contribute to the association between intelligence and suicidal behaviour. One way to investigate potential mechanisms is to separate factors early in life, such as psychiatric illness, personality aspects, psychological distress and social problems, and factors in adulthood, such as socioeconomic position and family formation. Individual factors such as psychiatric illness and personality aspects are commonly studied in relation to suicidal behaviour, but demographic factors are also important [149]. Considering previous hypotheses on mechanisms in the association between intelligence and health,

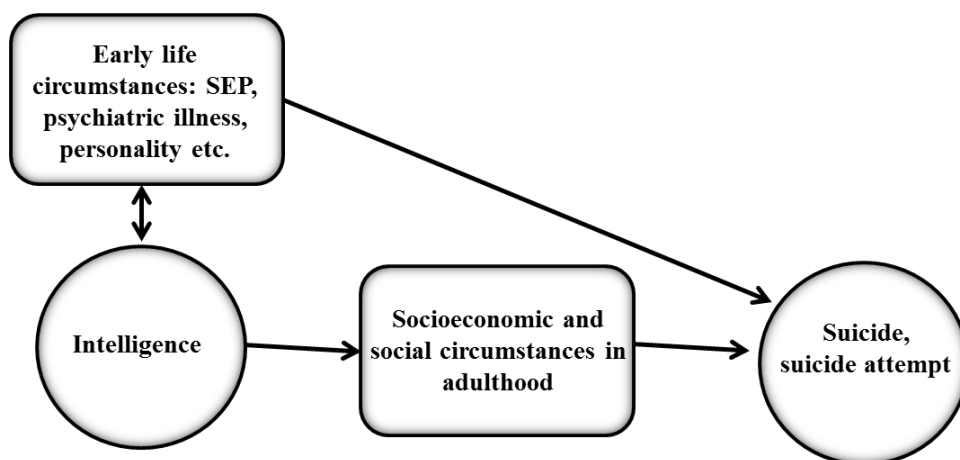


Figure 3. Pathway model of potential mechanisms underlying the association of intelligence with suicide and suicide attempt.

an adapted model is depicted in Figure 3. The explanatory factors correspond roughly to boxes 1 and 3 in the model of Whalley and Deary's four hypotheses in Figure 2. However, since intelligence can predict health outcomes from an early age, it is possible that intelligence also can affect psychological and psychiatric health and social problems, so an association between intelligence and such factors might run both ways. Suicide and suicide attempt are combined to simplify the model, but since they might be regarded as separate outcomes [149] it is appropriate to analyse them separately in statistical models.

Work-related health, work ability and disability pension

As we have seen, intelligence is associated with health in general, including psychiatric disorders [12,21,61,64], and perhaps also musculoskeletal disorders [58]. These are the two leading causes for disability pension, a benefit granted to people with medically certified reduced work ability due to illness or injury [156]. Intelligence is also associated with job performance [157]. Therefore, it is perhaps not surprising that intelligence has been found to predict disability pension in Sweden [158] and in Norway [159]. Similarly, work ability reduction and benefit payment due to long-standing illness was predicted by lower intelligence in British cohorts [160].

In addition to general associations between intelligence and health, authors suggest that other mechanisms might contribute to this specific work-related outcome. First, educational attainment, highly correlated with intelligence, has been found to be a mediator [159,160]. Lower education might lead to higher job insecurity and manual works, possibly increasing the risk for work-related illness and reduced work capacity [160]. Lower education might also limit the possibilities to transfer to a job that is compatible with the work capacity in case of disability or illness [160]. Second, the verbal component of higher ability might be associated with receiving better support from colleagues, managers and the private network, and being better able to speak for oneself in the contact with health care and social insurance professionals [160]. In these studies, there was limited control for explanatory factors. Furthermore, none of the previous studies have included disability pensions granted after age 43, whereas the number of disability pensions increase with age [156] and mechanisms leading to disability pension might differ according to age.

Traditionally, work-related factors are studied in relation to disability pension and other work-related health outcomes. In this perspective, intelligence would be regarded as a factor leading to more or less healthy work environments, which in turn might lead to or protect from disability pension. However, it is possible that some of the association is explained by factors that are more related to the individual than to the work circumstances, but it is difficult to separate these pathways since they are closely interrelated. One way to disentangle these pathways is to study factors prior to labour market entry separately from factors related to working life and socioeconomic position after labour market entry. Considering again the four hypotheses in Figure 2, an adapted model with disability pension as the outcome is depicted in Figure 4.

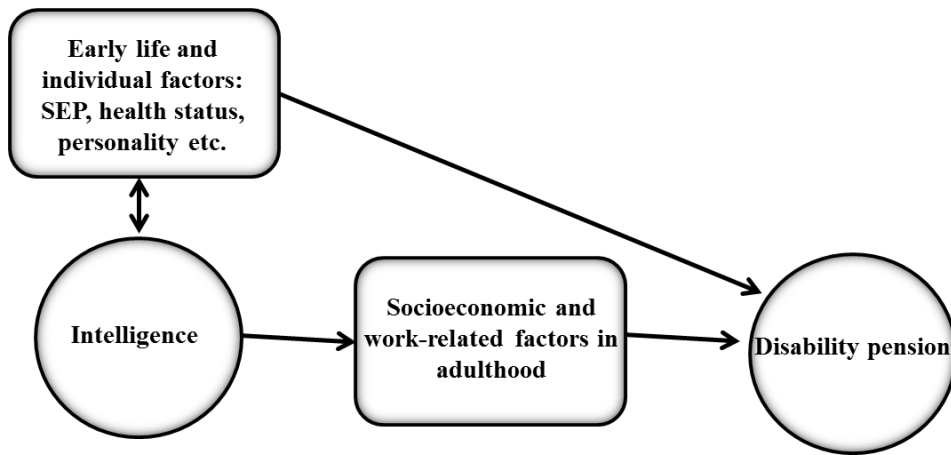


Figure 4. Pathway model of potential mechanisms underlying the association of intelligence with disability pension.

Health in youth

Many studies have investigated associations of early intelligence with various conditions in adulthood. The findings include diverse conditions and health indicators such as widespread pain [161], inflammatory markers [53,54], lung capacity [27,55], and self-reported general health [51].

It is unclear when the health disparities emerge, and what types of health disparities are present in young age. If the association is completely mediated by adult socioeconomic position, we would expect no association before labour market entry. On the other hand, if system integrity is an important explanation, we might expect health differences already at a young age. Functional somatic symptoms [162], inflammation [163], low physical fitness [116] and less healthy behaviours [30] in youth have been found to be associated with lower intelligence, indicating a propensity for poor somatic health, but somatic disorders have not been investigated.

Also, to our knowledge, only one previous study has reported on the associations of intelligence with a range of health outcomes at once. Der et al [58] reported the associations of adolescent intelligence with a range of self-reported health complaints at age 40 in a US cohort. They found that most conditions were less common with higher intelligence, such as ulcers, chest pain and asthma, but some were more common, including high cholesterol and thyroid trouble. Socioeconomic background had typically little or no impact on the estimates, but no other explanatory factors were included in the study.

Further explorations of somatic disorders in youth would contribute to a better understanding of the associations between intelligence and health. So far, little is known about when the health disparities relating to intelligence level emerge. Health status and diseases early in life in relation to intelligence level might be informative with regards to the hypothesis of bodily system integrity (hypothesis number 2 in section 1.3.1 and Figure 2). If system integrity is an important mechanism in the association between intelligence and health, it is possible that associations are present already at an early age. On the other hand, if circumstances in adulthood is the main

mechanism (hypothesis 3 in section 1.3.1 and Figure 2), we would expect little or no health disparities prior to labour market entry.

Intelligence in the presence of a disease

It has been suggested that intelligence is important for disease management. Associations of intelligence with health behaviours and lifestyle-related disorders such as the metabolic syndrome [47,48] and cardiovascular disease [34,35,36,37] in general populations suggests a link to health management. Furthermore, health literacy, denoting the ability to understand health information and make appropriate health decisions, has been put forward as a proxy for intelligence [72,130]. Health literacy has been found to predict mortality among older people with heart conditions [164]. This supports the hypothesis that intelligence is important in disease management [1,72,132]. This hypothesis is further supported by the findings that intelligence is associated with better adherence to medication in samples with an elevated risk for CVD [165,166] and with refill persistency among men prescribed with hypertensives (although no association was found for statins) [167].

Cardiovascular disease (CVD) is globally the major cause of death and accounts for the highest disease burden [168]. Some of the earliest studies on associations of intelligence with specific illnesses and causes of death investigated rates of cardiovascular disease and mortality, and more have followed [23,34,35,36,37,169,170,171,172]. Lifestyle modification and health behaviours are the most recommended preventive actions for CVD [173]. Thus, the hypothesis of diseases prevention and management as a mediator in the association is pertinent in CVD, supported by observations that intelligence is associated with health promoting behaviours [30,33,165,166], and inversely related to lifestyle-related risk conditions such as obesity and the metabolic syndrome [47,48,134,174]. Adjustment for health behaviours and indicators of poor health attenuated the association in some studies [34,169,171]. However, adjustment for education had a stronger attenuating impact in some studies [36,37,171,172], but to what extent this represents socioeconomic position or knowledge of health behaviours, or both, is unclear.

1.4 A LIFE COURSE APPROACH TO COGNITIVE EPIDEMIOLOGY

Life course epidemiology is the field in which risk factors for morbidity and mortality, biological as well as societal, are acknowledged across the course of life from early life and onwards [175]. Cognitive epidemiology fits well into this view, as intelligence is present throughout the life course; quite stable, but other factors can impact; associated with many factors during the life course that are associated with health; the importance of intelligence on health might vary across the life course; and confounding and mediating factors are important to disentangle, but this is not always easy. Three of the most common life course models of how risk factors across life affect health outcomes are shown in Figure 5 (adapted from Kuh et al [175]).

In the critical period model (a), an exposure occurs at a certain point in time and has a determinant role in the development of a disease that might not appear until much later in life. One example is that the perinatal environment can affect the risk for

cardiovascular disease in middle age [176]. In cognitive epidemiology, the notion of system integrity might fit into this model, as system integrity is supposed to develop very early in life and remain fairly unchanged while affecting both intelligence and health. Note, however, that in such a model system integrity would be the “true” exposure variable and intelligence only a marker.

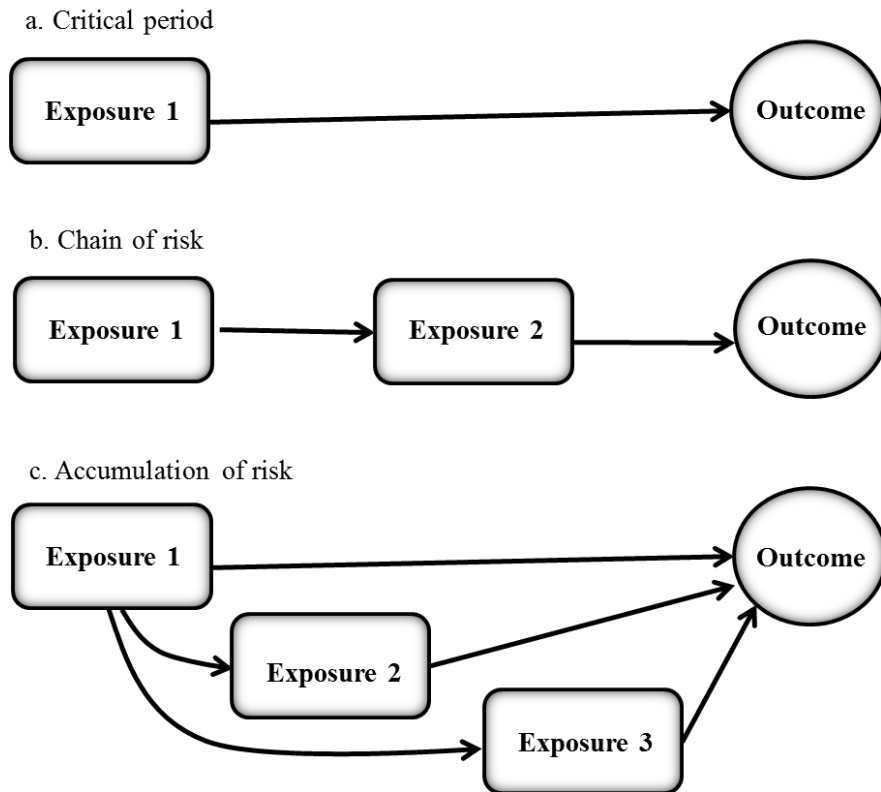


Figure 5. Models of associations between exposures and outcomes in life course epidemiology.

In the chain of risk model (b), one exposure is a risk factor for another factor (exposure 2), which in turn is the “true” cause for the outcome. An example would be if intelligence in itself does not affect the risk for morbidity or mortality, only the likelihood to attain a longer education and more advantageous positions in adulthood, which then would be associated with lower risks. This corresponds to the suggestion of mediation by adult position in Figure 2.

Accumulation of risks (c) occurs when the exposure affects other exposures across the life course, adding up to a higher risk for the outcome. This would happen if intelligence in itself affects the risk for morbidity or mortality, and also affects the likelihood to smoke and to have a certain socioeconomic position in adulthood, all acting in concert to increase or decrease the risk of poor health and early death.

2 AIMS OF THE THESIS

2.1 OVERALL AIM

The overall aim of this thesis is to increase the understanding of the association between early-life intelligence and morbidity and mortality, using a life course approach.

2.2 SPECIFIC AIMS

- To explore associations between intelligence and suicide and suicide attempt (study I).
- To examine if there is an association between intelligence and disability pension in middle age (study II).
- To examine to what extent associations between intelligence and health outcomes are explained by factors established early in life and in adulthood, respectively (study I and II).
- To explore associations between intelligence and health conditions in youth (study III).
- To examine if there is an association between intelligence and recurrence and mortality among men who are diagnosed with coronary heart disease (study IV).

3 METHODS

3.1 STUDY POPULATION

All four studies were based on the same cohort, the Swedish conscription cohort 1969-70, which was linked to several national registers, as described below. The record linkage was possible due to the unique personal identification number every Swedish citizen holds. However, all data was anonymised by Statistics Sweden before providing it for research, and the personal identifiers were replaced by randomly distributed identification numbers to allow for record linkage while still protecting the integrity of the individuals.

3.1.1 The Swedish conscription cohort 1969-70

Until the mid-1990's, all Swedish male citizens were obliged by law to present themselves for military service conscription, most often at about 18 or 19 years of age. Not everyone was picked out for the actual military service, but participation in the thorough assessment was mandatory. In 1969-70, only about 2-3% of the men were excused, mostly due to severe disability or congenital disorders. The cohort used in these studies consists of those men who underwent conscription during the period from autumn 1969 to spring 1970 and were born in 1949-51, and hence 18 to 20 years old at the time of conscription. Approximately 2% of the conscripts were born earlier and were excluded for homogeneity [15].

The conscription procedure took about two days and included physical and medical assessments, an interview with a psychologist, a test of intelligence, and a survey comprising two questionnaires about social background, psychological and psychosomatic problems, behaviour and adjustment, and substance use, including smoking, alcohol and illegitimate drugs. Several of the variables that were recorded during the conscription were selected for inclusion in the analyses in studies I-IV, based on their association with intelligence as well as health outcomes reported in previous studies.

Exposure variable: intelligence

In all studies, I-IV, intelligence was the exposure variable. Intelligence was assessed at conscription by four sub-tests. This battery had been developed by psychometricians over decades and was designed to measure general intelligence, g [177]. It was primarily used to predict the conscript's ability to profit from education in military training and finding the right level of learning demands [177,178].

The four tests were progressive, starting with easy questions and then increasing in difficulty. The logical-inductive test, "Instructions", took 12 minutes and contained 40 items, most of them instructing the test subject to follow instructions related to an array of shapes and letters of the sort: "Put a line through the square under the longest word". Some items required general knowledge, for example the location of Sweden in relation to Denmark, or arithmetic calculations. The verbal test, "Concept discrimination", took

7 minutes and contained 40 items, in which the test subject was asked to identify one word in a row of five that did not fit in, for example “admire” amongst “insist, request, question, believe”. The visuospatial test, “Paper form board”, took 12 minutes and consisted of 40 items. The test subject was asked to match a geometric shape to one of four clusters of triangles that could be put together to form the same shape. The technical–physical test, “Technical comprehension”, took 15 minutes and consisted of 52 items showing diagrams and pictures with accompanying questions and three response alternatives. The test subject was asked, for example, which of two bicycle wheels of different sizes would complete the most turns in 100 meters, or which of levers with different placements would most easily break [177,179].

The results were converted to standard-nine (stanine) scales with a normal distribution for each subtest, with scores ranging from 1 to 9. These were then combined and transformed into a new stanine scale as a global measure of general ability, corresponding to approximate IQ bands of: < 74, 74–81, 82–89, 90–95, 96–104, 105–110, 111–118, 119–126, > 126. The correlations between the subtests ranged from .50 to .75 [179,180]. Test-retest reliability in a group of 107 men, tested again after one to three years, was .81 for the global score [178]. In the cohort, 49 262 (99.9%) of the men had data on intelligence.

Covariates measured at conscription

In the physical examination, weight and height were measured and could be used to calculate body mass index (BMI, kg/m^2). It was used as a lifestyle-related risk factor for morbidity and mortality in studies II and IV. Height is often used as a proxy for socioeconomic circumstances in childhood, since for example nutrition affects growth [181], and was used as such in studies I and III. However, when interpreting the effect of height on associations between intelligence and any outcomes that are also correlated with height one should take into consideration that the height-intelligence correlation also has a genetic basis [182]. The erythrocyte sedimentation rate (ESR) was measured as a marker for inflammation, and was used as such in study III. The ESR has been found to correlate negatively with intelligence at conscription and predict mortality up to age 57 in this cohort [163]. ESR is less labile than many other markers and may better reflect chronic systemic inflammatory status [183]. Physical capacity was measured by a cycle ergometer test [184,185]. The conscript was instructed to maintain a pedal cadence between 60 and 70 revolutions per minute while the work rate was continuously until volitional exhaustion. The final work rate (W_{max}) was recorded, and divided by body weight. A W_{max} less than 205 W, representing stanine 1-3, was used as measure of low physical capacity in study III. Systolic and diastolic blood pressure (BP) was measured in a resting state, and used as risk factors for morbidity and mortality in studies II and IV.

The medical examination was performed by a medical doctor, who diagnosed any diseases and other disorders according to the International Classification of Diseases, version 8 (ICD-8), which was used in Sweden at that time. In any case of reported or suspected mental illness or psychiatric symptoms, the conscript was sent to a psychiatrist who made the psychiatric diagnosis (ICD-8 codes 295-310), if appropriate. Diagnostic groups based on all chapters in the ICD-8, and all single diagnoses given to

at least one thousand conscripts, were outcomes in study III. Musculoskeletal diagnoses (ICD- 8 codes 710-738) were used as a control variable in study II. Psychiatric diagnosis was used as a specific measure of psychiatric illness in adolescence, as a control variable in studies I, II and III, and as a secondary outcome in study III.

The interview with the specifically trained psychologist was structured according to a manual and took about 20-30 minutes [186]. An English summary of the interview process is provided by Lindqvist and Vestman [187]. The psychologist rated a few predetermined personality factors on five-point scales with normal distribution, based on the conscript's answers to question about how he had acted in the past, specifically related to adjustment, responsibility taken, and practical and emotional coping [178]. The personality factors "emotional control" and "social maturity" were included as control variables in studies I and II. "Emotional control" has been argued to be similar to constructs such as "emotional stability" and "neuroticism" (reversed) [180].

The questionnaires were made available for register linkage from this conscription year only. In study I, items designed to measure psychological distress and psychosomatic problems were included in the analyses as control variables. In study II and IV, items regarding alcohol use and smoking were used as measures of lifestyle risk factors for later health problems and included as control variables. A composite variable, risk use of alcohol, has previously been created by combining several alcohol-related questions: whether the conscript consumed ≥ 250 g 100% alcohol/ week, had ever been having an 'eye-opener' during a hangover, had been apprehended for drunkenness, or had 'often' been drunk (vs 'rather often', 'sometimes', or 'never'). An affirmative answer to any of these questions was coded as risk use of alcohol. One question dealt with current smoking, and the response alternatives was no, 1-5, 6-10, 11-20 or more than 20 cigarettes per day. In study II, this variable was condensed to four levels (no smoking, smoking 1-10, 11-20, or more than 20 cigarettes per day); and in study IV, the variable was condensed to three levels (no smoking, smoking 1-10, or more than 10 cigarettes per day) in order to increase power in the analyses as the sample was comparatively small.

3.1.2 National registers

Population and Housing Censuses

The National Population and Housing Censuses contain demographic information about individuals and households. They occurred about every fifth year during the greater part of the last century, until 1990 [188]. Thereafter, it was replaced by other means of data gathering.

In studies I-IV, socioeconomic position in childhood was included as a possible confounder in the association between IQ and health outcomes. It was based on the self-reported occupation of the head of household, generally the father, in 1960 when the men were about ten years old. Occupations were classified in six socioeconomic groups: (1) unskilled workers; (2) skilled workers; (3) assistant non-manual employees; (4) non-manual employees at intermediate or higher level; (5) farmers; (6) those not classified into any socioeconomic group, for example unemployed, early retired or

disabled. In study IV, with a smaller sample, the variable was transformed into three groups in order to retain statistical power: unskilled or skilled worker; non-manual employees at assistant, intermediate or higher level; and farmers, self-employed and those not classified. Information on crowded housing, classified as more than two people per room, not including the kitchen, was also recorded in the census. This variable was included as an indicator of socioeconomic circumstances in childhood, together with the occupation-based measure of socioeconomic position, in studies I and III.

Socioeconomic position in adulthood was included as a possible mediator in studies I, II and IV. Occupations were classified in eight socioeconomic groups, similar to the 1960 classifications but placing self-employed (mostly skilled workers or drivers) and non-manual employees at higher level in their own groups. In study I, occupation in 1985 at age 34-36 was used, and in studies II and IV occupation in 1990 at age 39-41 was used. In study IV, the variable was transformed into four groups to retain statistical power: workers; non-manual employees; farmers and self-employed; and those not classified.

In study I, information on family formation in 1985 was used as indicators of social circumstances that might be protective against suicide [189]. The variables used were whether the man was married or cohabiting versus living alone (similar information was obtained from the LOUISE/LISA data bases for study IV, see below) and whether any children under 15 years of age were living in the household.

LOUISE/LISA

Since 1990, data in administrative records related to labour market and socioeconomic circumstances for all Swedish citizens from age 16 and older is collected in The Longitudinal Database of Education, Income and Employment (Swedish acronym LOUISE[190]. It was renamed The Longitudinal Integration Database for Health Insurance and Labour Market Studies (Swedish acronym LISA) and extended in 2004 [191]. The databases are administered by Statistics Sweden.

In study II, disability pension granted 1991-2008, when the men were about 40-58 years old, was used as the outcome. Disability pension is granted by the National Social Insurance Agency to adults up to age 65 whose working capacity is permanently reduced by at least 25% due to a medically certified illness or injury [191]. Disability pension was registered at the end of each year in LOUISE/LISA.

Information on education, unemployment after 1990, income and sickness absence benefits were also obtained from the LOUISE database, and were included as control variables in study II. Information on income was also used in study IV. Education was categorized in five levels according to the highest education obtained by 1990: ≤ 9 , 10-11, 12-13, 14 and ≥ 15 years. Unemployment during the recession in Sweden in 1992-1994 was categorized into three groups of zero, 1-90 or > 90 days with unemployment benefit. Individual characteristics measured at conscription predicted unemployment during this period [192]. Income in 1990 was categorized in quartiles of the sum of income from employment, business and unemployment benefit. Sick leave in 1990 -

1991 was categorized in quintiles of the total number of days with sickness benefit, and was used as an indicator of reduced work capacity.

Information on whether the study participant was living in a single household was used in study IV, as a measure of social circumstances that might be related to CHD morbidity and mortality. The information was retracted from the year the man was hospitalized with CHD for the first time, that is, the year that the follow-up period started for the individual (see below). If no such information was available, due to for example case-fatality, information on single household was retracted from the year before the CHD event.

The Income and Tax Register

Information on unemployment before 1990 was obtained from the Income and Tax Register, and used as a measure of stability on the labour market in study II. The total number of years with any unemployment benefit between 1976 and 1990 was calculated for each individual and categorized in five groups: 0, 1-2, 3-5, 6-9 and >9 years in total.

The Swedish Work Environment Surveys and the Swedish Annual Level of Living Surveys

Work characteristics on occupational level were determined by classifications made from two national surveys. Job control was measured in the Swedish Work Environment Surveys 1989–1997 [193] and physical work load in the Swedish Annual Level-of-Living Surveys 1979–1981 [194], and based on these surveys all occupations in the Nordic Occupation Classification (NYK) were classified in two job exposure matrices by mean level of exposure [193,194]. In study II, the level of job control and physical work load was estimated by the individual's occupation registered in the Population and Housing Census 1990, and the variables were categorized in quartiles and used as control variables. These measures of job control and physical work load were presumed to provide a more precise estimation of work-related risk factors within occupational levels than the broader categories of socioeconomic position, and have previously been found to predict disability pension in this cohort [195].

The Patient Register

The national hospital discharge register is held by the National Board of Health and Welfare and contains information on nearly all admissions for psychiatric care from 1973 onwards, and has complete coverage on all inpatient care from 1987 onwards [196].

Suicide attempt was one of the main outcomes in study I, and was recorded in the register if it was followed by an overnight stay at the hospital. It was classified by the following ICD codes: E950–9 and E980–9 (ICD-8/9); X60–X84 and Y10–Y34 (ICD-10). This includes cases with undetermined intent. In study IV, information on diseases and conditions which are associated with poorer outcomes in CHD were included as comorbidity and complications. On basis of a model for such comorbidity [197], the following diagnoses obtained from the hospital discharge register up to 28 days after or

in the four years preceding the event were classified as either co-morbid conditions or complications: diabetes with complications, pulmonary edema, acute or chronic renal failure, cerebrovascular disease, malignancy, depression, cardiogenic shock, cardiac dysrhythmias, and congestive heart failure (ICD-codes are listed in the supplement of Study IV).

The Cause of Death Register

The national Cause of Death register is also held by the National Board of Health and Welfare and covers all deaths of Swedish citizens [198].

Suicide deaths was one of the main outcomes in study I. Deaths of undetermined intent were included, as previous studies have shown that most of these are likely to be suicides [199,200] and not including them might lead to an underestimation of suicides.

Deaths from the first CHD event (case-fatality), CVD and total mortality were secondary outcomes in study IV. In the sample of men with no previous CHD recorded in the patient register, case-fatality was defined as death with any underlying cause within 28 days of the first hospital admission for CHD, as is common in case-fatality research, or CHD as underlying cause in case of out-of-hospital death (ICD-9 codes 410-414; ICD-10 codes I20-I25). Mortality with ICD-9 codes 390-459 and ICD-10 codes I00-I99 as underlying causes, that is, all cardiovascular diseases, were classified as CVD mortality. Total mortality was defined as any mortality recorded in the register during follow-up. Mortality records for the men's parents were also linked to the data in study IV, and parental CVD death before age 65 was used as an indicator of heritable risk for early CVD.

3.2 STATISTICAL ANALYSES

In all four studies, intelligence level as measured at conscription was the exposure variable. In studies I, II and III, intelligence was modeled as a continuous variable using the stanine scale, with scores ranging from 1 to 9. In study IV, in which the study sample was smaller, intelligence was modeled in three categories: low (stanine score 1-3), medium (4-6) and high (7-9). Possible associations between intelligence and the outcomes were investigated using primarily two common regression techniques, survival analysis and logistic regression, described below. In all studies, covariates described above were added to the analyses in order to investigate their possible explanatory effect in the associations. For an overview of the variables used in the four studies, see Table 2.

Studies I-III were based on the full cohort, only excluding men with missing data on any variable included in the analyses, or who died prior to the beginning of follow-up in the longitudinal studies. For study IV, the study sample consisted of those men who obtained a first diagnosis of CHD (see the Patient register section above) between 1991 and 2007.

3.2.1 Survival analysis

In the longitudinal studies - I, II and IV – the associations between intelligence and the primary outcomes were estimated by calculating hazard ratios (HR's) and 95% confidence intervals (CI's), in Cox proportional hazard models using the PHREG procedure in SAS 9.2-9.3 (SAS Institute, Inc., USA). This model analyses time from the start of follow-up to the occurrence of an event, and assumes proportional risks over time. The proportionality assumption was assessed and confirmed by examining the log-log survival plot in all three studies.

In study I, the associations of intelligence at conscription with suicide 1971–2006 and first suicide attempt 1973–2006 were assessed. Thereafter, variables measured in childhood and at conscription were added to the model. The analyses were repeated with follow-up starting 1986, adding adulthood variables recorded in 1985 to the models. Men with a suicide attempt prior to 1986 were excluded from the analysis regarding later attempts. A sensitivity analysis was performed excluding men with a diagnosis of psychosis at conscription or in the patient register, since previous studies have shown that associations between intelligence and suicidal behaviour might be different among men with psychosis [17,40].

In study II, disability pension granted 1991-2008 was the outcome. The effects of adjusting for the control variables separately were investigated by adding them one by one to the model. The variables were then combined in two sets: one comprising variables recorded before or soon after presumed entry into the labour market, that is, up to and including conscription; and a second set comprising variables recorded in adulthood, when the men in the sample in most cases had entered the labour market. The effect of time period was assessed by dividing follow-up into two time periods, 1991-1999 and 2000-2008. The effect of adding work characteristics to the model was performed in a separate model in a subsample of men with data on these variables. The possible mediating role of exclusion from the labour market during the recession of the early 1990s in the association between intelligence and disability pension was investigated by adding sickness absence in 1991-92 and unemployment in 1993-94 to the model, with follow-up restricted to 1995-2008.

In study IV, those men who obtained a first CHD diagnosis between 1991 and 2007 were retracted from the cohort and constituted the study sample. Among these men, CHD recurrence was the primary outcome, defined as a second diagnosis of CHD in the patient register. Associations of intelligence with CVD mortality and total mortality as secondary outcomes were also assessed. In addition to adjusting for age in a basic model, early-life variables and variables measured at conscription or later in adulthood were added to the model. Thereafter, education in three levels, ≤ 9 , 10-12 and >12 years, was added to the model. Effect modification was investigated in stratified analyses. The following additional analyses were performed: the follow-up time was restricted to two years to remove any bias due to follow-up time differences; the time lag after the first event was prolonged from 28 days to six months to minimize the risk that a second diagnosis was a late effect of the first event; and a restriction was made to myocardial infarction (MI; ICD-9 410, ICD-10 I21-22), applied to both the inclusion criteria (first event) and outcome (recurrence). Also, an analysis was performed

combining recurrences and deaths from any causes as endpoints, since the higher mortality among people with lower intelligence constitutes a competing risk and might cause an underestimation of the intelligence-recurrence association.

3.2.2 Logistic regression

In study III and IV, logistic regressions were performed, estimating cross-sectional associations between intelligence and the outcomes by calculating the odds ratios (OR's) and 95% CI's, using the LOGISTIC procedure in SAS 9.2-9.3 (SAS Institute, Inc., USA).

In study III, associations between intelligence and diagnoses and health indicators at conscription were assessed. Socioeconomic factors early in life were controlled for by adding them to the model. An additional analysis was performed excluding men who obtained a psychiatric diagnosis at conscription, since psychiatric comorbidity might confound the associations.

In study IV, the association between intelligence and case-fatality at the first CHD event was estimated as a secondary outcome. A higher case-fatality rate among men with lower intelligence might affect the possible association between intelligence and CHD recurrence which was the primary outcome in this study.

3.3 ETHICAL CONSIDERATIONS

Ethical approval was obtained from Stockholm's Regional Ethical Review Board at Karolinska Institutet. All data was anonymised before it was made available and therefore, and because of the character of the data base, the normal requirement for written consent by study participants was waived. Still, it is of course important to handle the sensitive data that medical and death records entail carefully, in order to respect the integrity of the study participants and maintain the public trust in this type of research.

Furthermore, whether one is a study participant or not, one might find the aim of studying associations between intelligence and health as questionable, given the controversies regarding the use and interpretations of data in the history of intelligence research [201,202]. Also, the willingness to reduce inequalities might be lower when they are perceived as genetically and biologically based [203]. In the study design and performance of studies, and in presenting and discussing the results, one can mitigate mis- or overinterpretations that might contribute to inequality, for example by talking about these differences as inequalities in themselves that should be reduced (see for example Deary, Weiss and Batty [5]). Gaining a better knowledge of how intelligence is associated with health outcomes will hopefully, in the long term, provide us with answers how to reduce health inequalities and improve health overall.

Table 2. Overview of studies I-IV.

	Outcome and source	Description of study sample	Covariates	Main findings
Study I	Suicide: national cause of death register. Suicide attempt: national hospital discharge register.	44 560 men, followed 1971/73-2006, age about 20-57.	Childhood: Socioeconomic factors. Conscription: Social problems, personality aspects, psychiatric diagnosis, psychosomatic symptoms. Adulthood: SEP, family formation.	Intelligence was associated with later suicide and suicide attempt. Covariates, in particular social problems, personality aspects, psychiatric diagnosis and circumstances in adulthood contributed in attenuating the associations, but the gradients remained.
Study II	Disability pension: LOUISE/LISA register	44 144 men, followed 1991-2008, age about 40-59.	Childhood: SEP. Conscription: Personality aspects, health-related lifestyle factors, psychiatric and/or musculoskeletal diagnosis. Adulthood: education, SEP, income, work characteristics, unemployment, sickness absence.	Intelligence was associated with disability pension in middle age. The graded association was considerably attenuated but remained after adjustment. Socioeconomic factors in adulthood and, to a lesser degree, personality aspects contributed in attenuating the association.
Study III	Somatic diagnoses: conscription data (cross-sectional study)	49 262 men, age 18-20	Childhood: Socioeconomic factors. Conscription: Psychiatric diagnoses.	Lower intelligence was associated with a range of diagnoses/health indicators, while a few were less common with lower intelligence. However, psychiatric disorders had the strongest association with lower intelligence.
Study IV	Recurrence in CHD: national hospital discharge and cause of death registers	1923 men, followed from the date of first CHD diagnosis (1991-2007) through 2008, age about 40-59.	Childhood: parent's early CVD death, socioeconomic position. Conscription: BMI, smoking, risk use of alcohol, BP. Adulthood: SEP, income, single household, comorbidity.	Intelligence was not associated with the risk for CHD recurrence, but with all-cause and CVD mortality.

4 RESULTS

Here, a summary of each of the studies in relation to the specific aims is presented. Table 2 shows an overview of the results.

4.1 STUDY I: INTELLIGENCE AND SUICIDE AND SUICIDE ATTEMPT

We found a graded association of lower intelligence with higher risk of both completed suicide and suicide attempt. The associations were attenuated but remained after adjustment for several potential confounders and mediators. In particular, psychiatric diagnosis, social problems and personality aspects in youth and social circumstances in adulthood contributed in attenuating the associations.

Figure 6 shows the decreasing number of attempted and completed suicides per 1000 men with increasing intelligence level. No adjustments are made; for a graphical view of crude and adjusted OR's, see Study I, Figure 1.

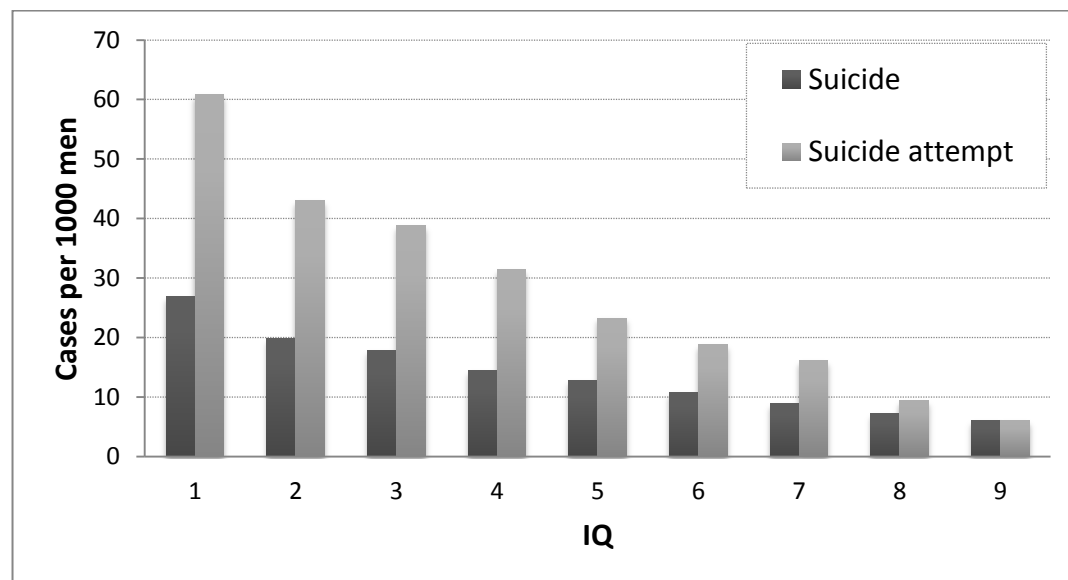


Figure 6. Attempted and completed suicides up to age 59 by IQ test performance at conscription.

Table 3 shows the prevalences of the covariates across the range of IQ on the stanine scale in the cohort. Most factors were graded, with more disadvantageous conditions typically being less prevalent with higher IQ. This includes, for example, low socioeconomic position in childhood (head of household in manual occupation), self-reported contact with police or child care authorities, low emotional control and social maturity assessed by conscription psychologists (rating 1-2 on the scale ranging 1-5), obtaining a psychiatric diagnosis, low socioeconomic position in adulthood (manual occupation), living alone and not having children in the household.

The crude (unadjusted) and adjusted associations between intelligence and suicide and suicide attempt during the full follow-up period are shown in table 4. In a repeated analysis among men who were alive in the beginning of 1986 and had data available on

Table 3. Description of the study sample (n=44 560). Prevalence of covariates in percent.

		IQ-score in stanine units								
		1 (low)	2	3	4	5	6	7	8	9 (high)
		N								
		1599	2266	4268	6267	7643	8035	6839	4694	2949
Childhood, adolescence and early adulthood (N)		%								
Low childhood SEP	24238	68.9	68.6	68.6	63.8	59.6	52.8	45.2	38.5	32.4
Crowded housing	9127	36.7	32.4	29.6	25.0	22.0	18.1	14.8	11.9	9.0
Short stature	4881	21.3	19.2	16.5	12.9	10.7	9.7	7.6	6.5	5.9
Contact with police or child care authorities	12791	37.8	38.3	36.3	34.4	31.7	26.9	24.1	19.2	16.4
Truancy	8092	22.5	20.8	19.6	17.8	17.9	17.2	18.2	17.7	16.6
Low emotional control	13336	61.2	46.3	38.0	33.7	28.3	26.1	23.8	22.9	20.8
Low social maturity	9764	61.9	41.5	32.2	26.5	20.0	17.2	13.7	12.6	12.0
Psychiatric diagnosis	4833	37.0	19.2	15.2	11.6	10.3	8.6	7.3	6.4	5.3
Gets angry easily	17190	51.2	51.5	48.5	43.6	40.2	36.9	32.7	29.8	24.8
Feeling “down”	9417	26.5	24.6	22.5	21.2	20.9	20.2	20.5	19.9	19.9
Nervous	14572	46.3	42.8	38.6	35.5	32.8	30.6	29.3	27.5	24.8
Worried and restless	8611	21.9	20.1	19.2	19.9	19.9	18.9	19.0	18.4	18.3
Irritated under time pressure	18096	57.5	54.1	50.6	45.8	42.5	38.7	34.7	31.1	24.8
Insecure	10892	32.1	24.5	23.6	23.1	23.8	24.0	24.3	25.4	26.0
Sensitive	5791	12.1	9.3	8.9	9.9	11.1	13.6	15.2	17.6	19.8
Nervous medication	4996	16.3	14.5	13.2	11.6	11.2	10.5	10.0	10.3	8.5
Headaches	13187	45.6	39.5	34.4	31.5	29.7	26.8	26.6	25.2	23.9
Stomach problems	8718	26.6	24.7	23.7	22.2	19.4	18.2	17.9	16.0	13.8
Difficulties falling asleep	11991	36.9	33.3	30.0	27.1	26.3	25.4	24.8	25.4	24.8
Adulthood, age 34-36(N)		%								
Low adult SEP *	17646	71.9	68.3	65.9	58.2	49.7	35.3	25.3	17.5	10.9
Unmarried/living alone *	10984	45.4	34.0	28.4	27.3	24.7	23.3	21.5	21.3	20.7
No children in household *	21050	71.1	60.7	54.9	52.4	49.1	47.3	44.5	43.6	42.3

* Prevalence among men with information on adulthood as well as earlier variables (N= 43 479).

socioeconomic and social circumstances in 1985, when the men were about 34 years old, the associations were of similar magnitude (HR and 95% CI for suicide: 1.19, 1.13-1.25; suicide attempt: 1.25, 1.20-1.31). The association was attenuated when factors in childhood and early adulthood were added to the model (see variables in table 3) to the model (HR and 95% CI for suicide: 1.14, 1.07-1.21; suicide attempt: 1.19, 1.13-

Table 4. Associations between intelligence at conscription 1969-70 and suicide 1971-2006 and suicide attempt 1973-2006. Crude and adjusted hazard ratios, with 95 % confidence intervals, per 1 point decrease in intelligence score on the stanine scale.

	Suicide 1971-2006		Suicide attempt 1973-2006	
	N= 44 560, 553 cases		N= 44 469, 1058 cases	
	HR	95%CI	HR	95%CI
Crude	1.20	1.15-1.24	1.28	1.25-1.32
Adjusted for:				
Childhood socioeconomic factors*	1.18	1.13-1.23	1.28	1.24-1.32
Contact with police or child care authorities	1.16	1.12-1.21	1.23	1.20-1.27
Truancy	1.19	1.14-1.24	1.27	1.24-1.31
Emotional control	1.15	1.10-1.20	1.21	1.18-1.25
Social maturity	1.14	1.09-1.19	1.19	1.16-1.23
Psychiatric diagnosis at conscription	1.16	1.11-1.20	1.23	1.19-1.27
Psychological and somatic symptoms **	1.18	1.13-1.23	1.24	1.21-1.28
Adjusted for all factors in childhood and early adulthood	1.12	1.07-1.18	1.17	1.13-1.21

*Socioeconomic position, crowded housing, height

** Self-reported: gets angry easily, often feeling "down", nervous, worried and restless, irritated under time pressure, insecure among others, sensitive, has taken "nervous medication", having headaches, stomach problems or difficulties falling asleep.

1.25). Likewise, the associations were attenuated when socioeconomic position, civil status and having no children in the household were added to the model (HR and 95% CI for suicide: 1.12, 1.06-1.19; suicide attempt: 1.17, 1.12-1.22). In a fully adjusted model including all factors from childhood to adulthood, the associations were slightly attenuated further (HR and 95% CI for suicide: 1.10, 1.04-1.18; suicide attempt: 1.14, 1.09-1.20).

4.2 STUDY II: INTELLIGENCE AND DISABILITY PENSION

We found a graded association between lower intelligence and a higher risk for a being granted a disability pension between ages 40-59. Socioeconomic and work-related circumstances in adulthood, including unemployment, education, socioeconomic position and income explained much of the association. In addition, factors measured already in late adolescence also contributed in explaining the associations, for example emotional control, social maturity, smoking, risk use of alcohol, high BMI and psychiatric illness. All factors combined attenuated the association considerably, but an 11% higher risk per step decrease on the stanine scale still remained after adjustments (table 5).

Job control and physical workload had no impact on the association between intelligence and disability pension, over and above the effects of the other factors (fully adjusted HR, 95% CI 1.11, 1.09-1.13 in models including or excluding job control and physical workload, in a subsample of 39 714 men with such data). The number of

Table 5. The association between intelligence at conscription 1969-70 and disability pension granted 1991-2008. Crude and adjusted hazard ratios, with 95 % confidence intervals, per 1 point decrease in intelligence score on the stanine scale. Adjustments are made for each variable separately and in combinations of variables by stage in life.

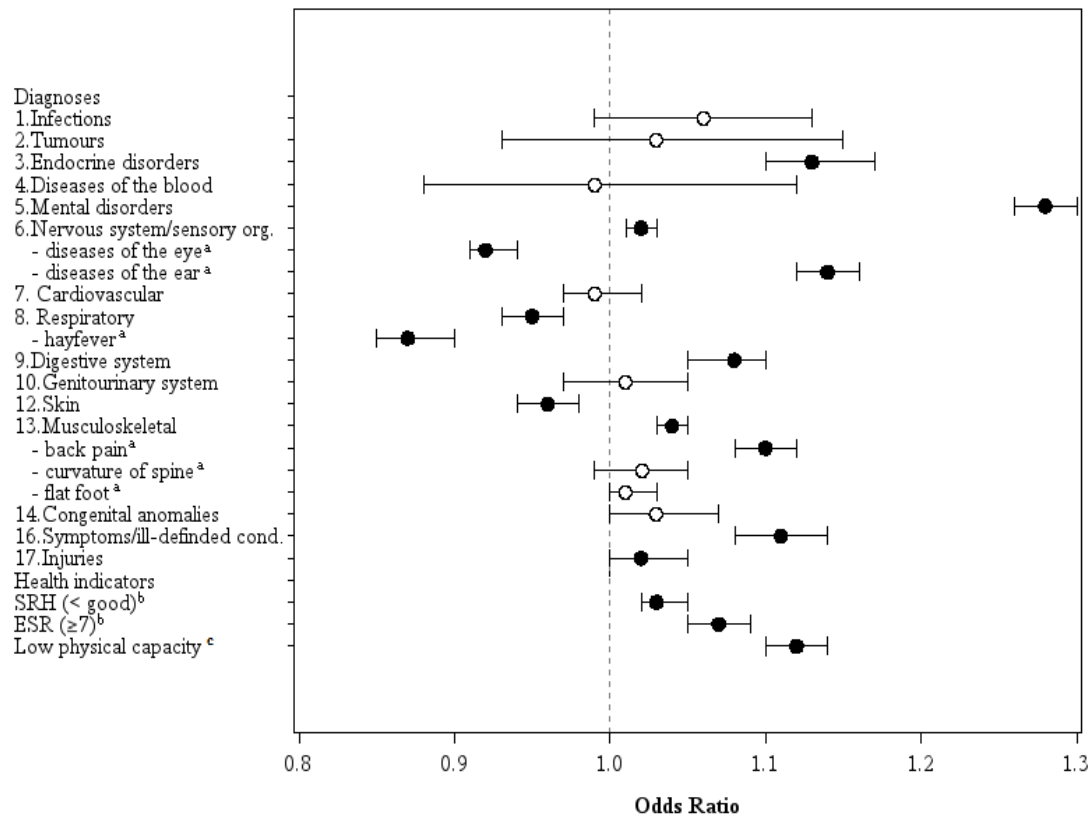
Disability pension 1991-2008		
<i>N= 44 144; 4 899 disability pensions granted.</i>		
	HR	95%CI
Crude	1.26	1.24-1.27
Adjusted for:		
A. Before labour market entry		
Childhood SEP	1.25	1.23-1.27
Personality factors (emotional control, social maturity)	1.21	1.19-1.22
Health lifestyle factors (smoking, risky use of alcohol, BMI)	1.23	1.21-1.25
Psychiatric diagnosis at conscription	1.23	1.21-1.24
Musculoskeletal diagnosis at conscription	1.25	1.24-1.27
All factors before labour market entry	1.19	1.17-1.21
B. Adulthood, after labour market entry		
Unemployment 1974-90 (years with benefits, 5 groups)	1.22	1.20-1.23
Education	1.19	1.17-1.21
Adulthood SEP	1.20	1.18-1.21
Income	1.19	1.17-1.20
All adult factors, after labour market entry	1.13	1.11-1.15
A+B: Full adjustment	1.11	1.09-1.13

sickness days 1990-91 and the number of unemployment days 1992-1994 had only a small impact on the association, when added to a fully adjusted model (HR, 95% CI 1.11, 1.09-1.13 adjusted for all other factors; HR, 95% CI 1.09, 1.07-1.11 including sickness absence and unemployment, in a subsample of 42 234 men followed from 1995 to 2008).

4.3 STUDY III: INTELLIGENCE AND SOMATIC HEALTH IN YOUTH

We found that lower intelligence was associated with several diagnostic groups, diagnoses and indicators of poor health (Figure 7; unadjusted results are shown in Study III). Lower intelligence was associated with a lower risk for a few diagnoses and diagnostic groups, while several were not associated with intelligence. Socioeconomic factors in childhood had generally no or minimal effect on the estimates, indicating that differences in socioeconomic background did not explain the associations.

In order to investigate the possibility that psychiatric comorbidity would underlie some of the associations, we repeated the analysis in a sample excluding men who also obtained a psychiatric diagnosis. The results were practically similar, indicating that



^a Single diagnoses, n >1000

^b SRH: self-rated health; ESR: erythrocyte sedimentation rate

^c Wmax; 1-3 vs 4-9

Figure 7. Associations of intelligence with diagnoses and health indicators at conscription, in OR's per step decrease on the stanine scale, adjusted for socioeconomic background (parent's occupation, crowded housing, height). Horizontal lines represent 95% CI's. Filled circles indicate statistical significance at the 0.05 level. N=47741.

psychiatric illness did not explain the associations. However, the association of lower intelligence with psychiatric diagnoses (“mental disorders”, in ICD-8) was stronger than the associations between intelligence and any of the somatic diagnoses or health indicators.

4.4 STUDY IV: INTELLIGENCE AND PROGNOSIS IN CORONARY HEART DISEASE

In a subsample of those 1923 men in the conscription cohort who had a first CHD event after 1990 and survived, intelligence measured in youth was not associated with the risk for recurrence. Contrary to the hypothesis, the risk for recurrence was not dependent on intelligence level. Table 6 shows HR's for recurrence in groups based on stanine scores; stanine 7-9 is termed high IQ, 4-6 medium IQ, and 1-3 low IQ.

By contrast, men with medium and low intelligence level had a higher all-cause and CVD mortality and case-fatality rate than men with high intelligence. They also had a higher case-fatality rate at the first CHD event. Adjusting for risk factors measured across the life course attenuated the associations somewhat (table 7).

Adjusting for education had no impact on the risk for CHD recurrence. Restricting the study group to men with MI showed a similar pattern, although statistical power was low due to the smaller number of events (fully adjusted HR, 95% CI for medium IQ: 0.96, 0.65-1.43; low IQ: 0.93, 0.59-1.46). There was no clear evidence of effect modification in stratified analyses, but statistical power was low in most of these analyses because of the small number of events in the stratified groups.

In an analysis with a minimum of six months' time lag after the first CHD event (yielding 660 recurrent events), performed in order to minimise the risk of including diagnoses related to the first event among recurrences, the HR's for recurrent CHD were slightly higher compared to the main analysis but were attenuated towards the null in the fully adjusted model (age adjusted HR, 95% CI for medium IQ: 1.06, 0.88-1.29; low IQ 1.17, 0.94-1.45; fully adjusted HR, 95% CI for medium IQ: 0.98, 0.80-1.20; low IQ 1.05, 0.83-1.33).

Table 6. Intelligence (IQ) and recurrence among survivors of a first CHD event 1991-2008. Follow-up time: mean 655, median 184 days.

Adjusted for	CHD recurrence. <i>N</i>=1923, 902 cases			
	HR	95% CI		
	High IQ (ref.)	Medium IQ	Low IQ	
Age	1	1.02 0.87-1.20	1.14 0.95-1.38	
+ Early life factors*	1	1.03 0.87-1.22	1.16 0.96-1.40	
+ Traditional CVD risk factors, conscription **	1	0.99 0.84-1.17	1.10 0.92-1.33	
+ Socioeconomic and social factors in adulthood ***	1	0.99 0.84-1.18	1.08 0.88-1.31	
+ Comorbidity/complications †	1	0.98 0.83-1.16	1.09 0.89-1.34	

* Childhood socioeconomic position, parent's CVD death at age <65.

** BMI, smoking, risk use of alcohol, systolic blood pressure.

*** Socioeconomic position, income, and single household.

†Comorbidity: Diabetes with complications, pulmonary edema, acute or chronic renal failure, cerebrovascular disease, malignancy, and depression; complications: cardiogenic shock, cardiac dysrhythmias, and congestive heart failure.

Table 7. Intelligence (IQ) and case-fatality at first CHD event 1991-2007 and subsequent mortality. High IQ is the reference in all analyses.

	28-day case-fatality		CVD mortality (mean 1919 days of follow-up)		All-cause mortality (mean 1816 days of follow-up)	
	<i>N=2156, 233 cases</i>		<i>N=1923, 74 cases</i>		<i>N=1923, 146 cases</i>	
	OR (95% CI)		HR (95% CI)		HR (95% CI)	
Adjusted for	Medium IQ	Low IQ	Medium IQ	Low IQ	Medium IQ	Low IQ
Age	1.33 (0.93-1.90)	1.46 (0.98-2.18)	1.94 (0.97-3.88)	2.32 (1.12-4.85)	1.74 (1.08-2.80)	2.20 (1.33-3.64)
+ Early life factors *	1.31 (0.91-1.88)	1.42 (0.94-2.14)	2.01 (1.00-4.06)	2.48 (1.17-5.27)	1.76 (1.09-2.84)	2.23 (1.33-3.73)
+ Traditional CVD risk factors, conscription **	1.16 (0.80-1.67)	1.18 (0.78-1.80)	1.87 (0.92-3.82)	2.22 (1.03-4.77)	1.61 (1.00-2.61)	1.96 (1.16-3.31)
+ Socioeconomic and social factors in adulthood ***	1.08 (0.74-1.57)	0.98 (0.62-1.52)	1.77 (0.87-3.60)	1.91 (0.87-4.20)	1.49 (0.92-2.43)	1.57 (0.91-2.69)
+ Comorbidity, complications †	1.06 (0.73-1.55)	0.97 (0.62-1.50)	1.92 (0.94-3.94)	1.98 (0.89-4.37)	1.63 (1.00-2.65)	1.62 (0.94-2.78)

* Childhood socioeconomic position, parent's CVD death at age <65.

** BMI, smoking, risk use of alcohol, systolic blood pressure.

*** Socioeconomic position, income, and single household.

†Comorbidity: Diabetes with complications, pulmonary edema, acute or chronic renal failure, cerebrovascular disease, malignancy, and depression; complications: cardiogenic shock, cardiac dysrhythmias, and congestive heart failure.

5 DISCUSSION

In summary, intelligence measured in youth was associated with various health-related outcomes in this cohort of Swedish men, such that lower intelligence was associated with higher risks for adverse outcomes, but there were also exceptions. Intelligence was inversely associated with suicide attempt, suicide and disability pension in adulthood in studies of the full cohort of about 49 000 men. In a subsample of those 1923 men who obtained a diagnosis of CHD after age 40, intelligence was not associated with the risk for recurrence (although intelligence was associated with the risk of obtaining the first diagnosis and thus be included in the sample), but was associated with mortality. Adjusting for covariates attenuated the associations that were found, but not fully; considerable parts of the associations typically remained after full adjustment. In cross-sectional analyses of associations of intelligence with diagnoses and other health indicators at conscription, at age 18-20, most diagnoses and all three indicators of poor health were inversely associated with intelligence, but a few diagnoses were more common with higher intelligence.

Of the covariates, personality aspects and psychiatric diagnosis at conscription, and socioeconomic and social circumstances in adulthood, were clearly contributing to the associations of intelligence with suicidal behaviour (study I) and disability pension (study II). Self-reported contact with police and child care, an indicator of social problems, was also contributing to the association with suicidal behaviour (study I). Health lifestyle factors, including smoking, risky use of alcohol and BMI, contributed to the associations with disability pension (study II) and case-fatality and mortality among men with CHD (study IV). Work- and labour market factors – unemployment, job control, physical strain and sickness absence – had little or no impact on the association with disability pension (study II). Socioeconomic factors in childhood did not contribute in any of the associations between intelligence and the studied outcomes (studies I-IV).

5.1 THE FINDINGS IN RELATION TO OTHER STUDIES

5.1.1 Intelligence and suicidal behaviour

The finding that intelligence predicted suicide and suicide attempt was in accordance with previous studies on male and gender-mixed populations [17,20,38,39,40,68,150]. However, associations have been different in other populations. In the UGU cohort, women and men were analysed separately, and there was no evidence of a higher risk for suicide with lower intelligence in women (but the number of suicides among women was low, leading to lower statistical power [40]). Null findings, or a lower risk with lower intelligence, have also been reported in men with psychoses and schizophrenia regarding attempted and completed suicide [17,40,204]. In a British birth cohort, higher intelligence at age 8 was associated with a higher risk for suicidal thoughts, plans and self-harm among boys, and with non-suicidal self-harm (but not suicidal outcomes) among girls, at age 17 [69]. Chang et al suggest that the etiology

differs from adult suicidal behaviours, and that adults with higher intelligence might use other means of coping with psychological distress [69].

An attenuating effect of adjusting for psychiatric illness in youth was previously found in a Danish conscription cohort [38], in line with our findings. However, the Danish study did not focus specifically on intelligence and related covariates. Self-reported contact with the police or child-care authorities, interpreted here as an indicator of maladjustment, also had an attenuating impact. Similar indicators have been investigated in other cohorts. Conduct problems in childhood, rated by parents and teachers, attenuated the association between childhood intelligence and self-reported suicide attempts up to age 25 in a New Zealand cohort [68]. By contrast, self-reports of childhood externalizing behaviour had no impact on the association between intelligence at age 14 and suicide attempts up to age 21 in an Australian cohort [150].

The attenuating effect of personality on the associations of intelligence with suicidal behaviour is a novel finding. The role of personality in the association of intelligence with all-cause mortality has however been studied. In a cohort of Scottish men and women, the association of intelligence in childhood with mortality up to age 67 was attenuated but remained significant in a model adjusting for dependability, a variable combining teacher ratings of perseverance, stability of moods and conscientiousness made by teachers [13]. In the Vietnam Experience Study on US males, intelligence and neuroticism (similar to our measure of emotional control) interacted such that the association between intelligence and mortality was stronger with increasing neuroticism, but no mutual adjustments were reported [142].

5.1.2 Intelligence and disability pension

Previous studies of risk factors for disability pension in Scandinavian male conscripts, followed to age 43 at most, showed that lower intelligence was associated with a higher risk [158,159]. The association across the full range of intelligence was investigated in only one of these, a Norwegian cohort, and in line with our findings there was a gradient [159]. None of the studies investigated mechanisms underlying this particular association.

Since societal systems for benefits in the case of reduced work ability due to illness or injury differ between countries, the number of studies on intelligence and disability pension is small. However, a study on three British cohorts showed that lower intelligence in childhood was associated with self-reported incapacity benefits and not being able to work because of permanent sickness or disability [160].

Unemployment is a related work-life outcome. In a study of 600 men and women on Northern Ireland in the early 1980's, an association of intelligence with unemployment among men and women on Northern Ireland was completely diminished when social background, school grades and personality (according to the Eysenck three dimension model) were taken into account [205]. Comparatively, we found that background and individual factors, including personality, contributed at least partly to the association of intelligence with disability pension.

5.1.3 Intelligence and somatic health in youth

Previous studies on the Swedish conscription cohort 1969-70 have reported associations of lower intelligence with lower physical capacity [116], higher ESR [163], and musculoskeletal disorders [206]. However, the range of diagnoses and health indicators was not investigated previously.

In one study on Dutch girls and boys, an association was found between lower intelligence and self-reported somatic symptoms up to age 16 [162], in addition to mixed findings on intelligence and mental health in adolescence [63,65,68,69,150]. Studies of somatic health in adulthood and old age in relation to intelligence are more common. One study, using the US National Longitudinal Study of Youth, reported on the associations of adolescent intelligence with a range of health complaints at age about 40 [58]. Although the self-reported conditions are not directly comparable to the diagnoses and health indicators in the conscription data, the longitudinal design of the study minimizes the risk for reverse causality, that is, poor health affecting cognitive ability and IQ test performance. Similar to our findings, lower intelligence was generally associated with poorer health, while some adverse health conditions were instead less common with lower intelligence.

5.1.4 Intelligence and prognosis in coronary heart disease

The association of intelligence with CVD morbidity and mortality had been reported previously [23,34,35,36,37,169,170,171,172], but this was the first study to investigate the role of intelligence in youth for prognosis in CHD. Since intelligence has been suggested to be important in health- and disease management [1,72,132], we hypothesized that pre-morbid intelligence would be associated with recurrence in men with CHD. Our null finding can be thought to contradict previous findings that intelligence was associated with medical adherence and prescription refill in samples with CVD or an elevated risk for CVD [165,166,167]. However, other studies found no association between lower cognitive ability and poorer medical adherence in schizophrenia and bipolar disorder [207].

Nevertheless, studies of the role of pre-morbid intelligence in chronic disease are still few and more studies are needed. There are some studies using a related construct, health literacy, denoting the ability to understand health information and make appropriate health decisions [72,131]. A recent review study found that the evidence of an association between health literacy and medical adherence is limited and inconclusive [208].

The associations of intelligence in youth with CVD and all-cause mortality are established in general populations [23,34,35,36,37,169,170,171,172], and we found that the risk for mortality from CVD and all-cause mortality increased with decreasing IQ also among middle-aged men with CHD. Similar to findings in general populations [34,35,36,37,169,171,172], factors early in life were not found to contribute to the

associations while health-related behaviours and socioeconomic factors in adulthood attenuated the associations when they were included in the models.

5.2 THE FINDINGS IN RELATION TO THE FOUR HYPOTHESES

The four suggestions initially outlined by Whalley and Deary [1](see also Figure 2) have been an underlying theme in the studies. First, associations between intelligence and later health might be confounded by circumstances and events early in life [1]. The results in these studies do not support the notion of childhood SEP as confounder, but some of our variables might be markers for other adverse circumstances. For example, self-reported contact with police and child care authorities suggests either an adverse home environment during upbringing, or maladjustment which might have causes in the home environment (shared environment, in twin studies) in addition to other environmental and genetic effects [209,210].

Second, bodily system integrity might underlie the associations [1,124]. This suggestion was partly addressed in study III. The findings, however, lend limited support for this hypothesis. If system integrity was a major factor in the association, we might have expected stronger associations for certain diagnoses, such as cardiovascular diagnoses and congenital anomalies, and stronger and more robust associations in general for the somatic diagnoses in comparison with psychiatric diagnoses. On the other hand, the definitions of system integrity and how it would be expressed is somewhat unclear [124]. We cannot exclude the possibility that the effects of poorer system integrity are long-term, expressed in for example CVD risk and early aging, or that they affect mental health.

Third, higher intelligence might be a pathway to healthier circumstances, for example a higher socioeconomic position [1]. In the studies I, II and IV which included socioeconomic and social circumstances in adulthood, these factors were consistently among the most impactful on the associations between intelligence and the outcomes. The associations of intelligence with suicide and suicide attempt were attenuated about a third; disability pension about half; and the associations of intelligence with case-fatality, CVD mortality and all-cause mortality in the subsample of men with CHD were also considerably attenuated when these factors were included in the models. Thus, these results confirm previous findings that circumstances in adulthood seem to be important mediators in the associations of intelligence with morbidity and mortality. Previous studies have typically included only socioeconomic measures in the models; here, we added social circumstances in form of civil status and children, and found that they might contribute as well.

Fourth, people with higher intelligence might be better at managing their health and any diseases they might have [1,132]. Our findings suggest that health behaviours in adolescence, indicated in our studies by self-reported smoking, alcohol use and BMI measured at conscription, have some explanatory role in the associations of intelligence and later health. These factors attenuated the association between intelligence and disability pension in the full cohort in study II, and also the association of intelligence

with mortality, particularly case-fatality, in the subsample of men with CHD in study IV.

However, the finding that intelligence was not related to the risk of recurrence in CHD among these men does not support the hypothesis that pre-morbid intelligence is important for disease management. This hypothesis should be investigated further in other samples. For example, it is possible that intelligence is associated with medical adherence but not with other important behaviour changes, such as healthy diets and physical activity. In a longitudinal study of 369 Swedish women, higher intelligence in youth was not associated with behaviour change after a medical exam in middle age at a conventional level of statistical significance, although there was a positive tendency [135]. Similarly, intelligence in adulthood (measured by verbal ability, which is more robust to cognitive decline than many other aspects of cognitive ability) was associated with health behaviours in cross-sectional analyses but not with improved health behaviours over time in an Australian community survey of about 6400 women and men, leading the authors to suggest that behaviour change might be more related to contextual and societal factors rather than individual intelligence [31]. Other possibilities is that since intelligence is associated with the risk of CHD in middle age, men with high intelligence who obtain a diagnosis of CHD in middle age might have other, unknown risk factors that are not related to intelligence level in this group; or that the health care the men received, which is given according to the individuals' need, compensated for differences in ability.

5.3 FURTHER INTERPRETATIONS OF THE FINDINGS

The findings from these studies can also form a more complex picture than the one depicted by Whalley and Deary in the emergence of this research area [1] (see also Figure 2). In a later model presented in Batty, Deary and Gottfredson's review paper in 2007 [123, p.284], psychiatric illness is included, both as an antecedent of lower intelligence and as a mediator on the path between intelligence and mortality.

Psychiatric illness had a role in our studies: psychiatric diagnoses at the conscription screening contributed in explaining the association of intelligence with suicide and suicide attempt, which both are closely related to more proximal psychiatric illness as a risk factor [149]. It also contributed to the association of intelligence with disability pension, and psychiatric disorders are one of the major causes for disability pension [156]. So, even though the contributions were modest, psychiatric illness was indeed related to the associations between intelligence in early adulthood and these outcomes; but causality cannot be determined in these studies.

The same can be said about the other contributing covariates from conscription. Personality aspects (emotional control and social maturity), social problems or maladjustment (indicated by self-reported contact with police and childcare authorities), and health behaviours (indicated by smoking, risky use of alcohol and BMI) were all associated with intelligence at conscription, and contributed to various degrees to the associations between intelligence and suicidal behaviour and disability pension. Health behaviours, or health status, at conscription also contributed to the

associations of intelligence with case-fatality in CHD and mortality among survivors of the CHD event. All these covariates might hypothetically be affected by intelligence; affect intelligence or IQ test performance; or they might be markers for some unknown factors that affect intelligence as well as the covariates.

Importantly, however, the graded associations remained to a large part after adjustment for the range of possible confounding or mediating variables.

A conceptual model of the findings in studies I-IV is depicted in Figure 8. All factors measured at conscription could hypothetically be affected by, or affect, intelligence (or intelligence test performance). Interrelations between the covariates are not depicted for practical reasons, but are assumed to exist.

Starting with somatic disorders and other health indicators which were the outcomes in study III, the underlying mechanisms for the association with intelligence probably vary between diagnoses. For example, the association between lower intelligence and a higher risk for back pain might be explained by a higher proportion of men who had already begun in a manual occupation among those with lower intelligence; more psychological distress and psychosocial problems among those with lower intelligence, since such factors are associated with back pain in youths [211]; or that back pain have an adverse impact on cognitive function and test performance [212]. However, intelligence at age 11 has been found to predict chronic pain in middle age, suggesting that intelligence might precede pain [161]. Impaired hearing on the other hand,

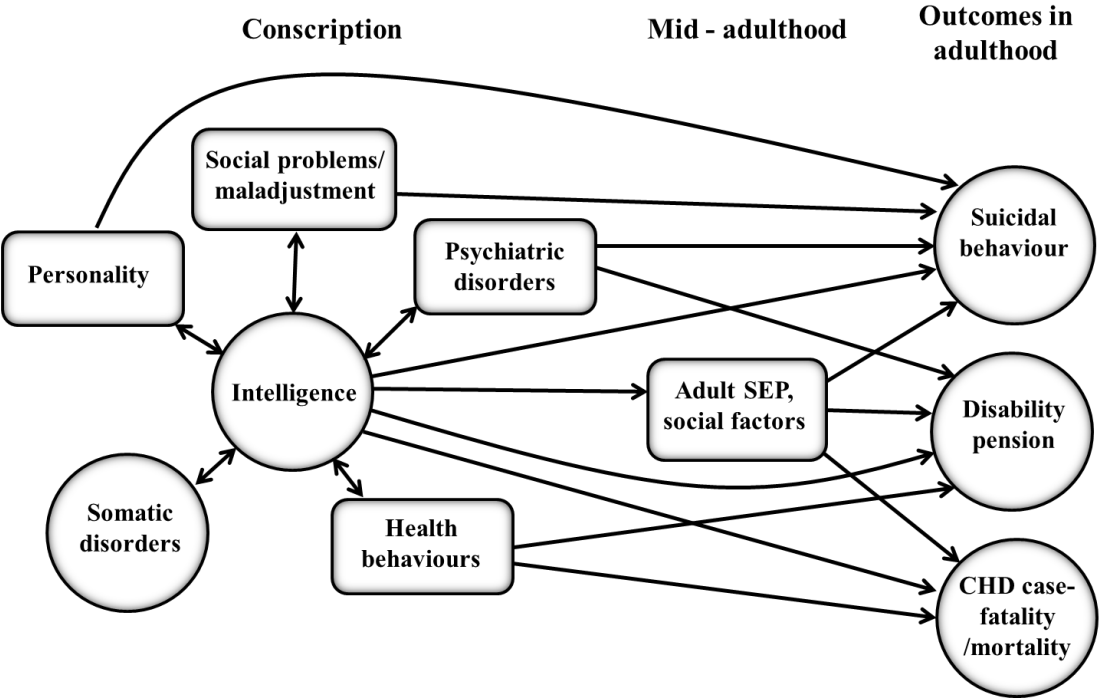


Figure 8. Pathway model of the associations between intelligence, the covariates and the outcomes in the four studies. Note that somatic disorders at conscription is one of the outcomes. Assumptions of causality between intelligence and other conscription variables are hypothetical and based on the literature.

which is the most common ear diagnosis in the cohort, might affect intelligence since our hearing is important in our cognitive development [213,214], while a lower risk for reduced eyesight with lower intelligence has been suggested to be applicable to early life experiences or pleiotropic genes [215].

Personality aspects were important explanatory factors in the associations of intelligence with suicidal behaviour and disability pension. Emotional control and social maturity are not part of any widely used personality models such as the Big Five, but have been compared to neuroticism and conscientiousness, respectively [180]. Associations between intelligence and personality have been found previously, but the magnitude and direction of the associations vary between studies and the bases for the associations are unclear [143]. It has been suggested that associations between intelligence and personality are attributable to differences during assessment rather than true personality traits, for example by differences in test anxiety or persistence [216], but contradictory findings also exist [217]. There is evidence suggesting that pleiotropic genes, affecting both intelligence and personality aspects, might underlie the associations [218,219].

Another suggestion is that personality aspects related to high stress reactivity, such as neuroticism and low emotional control, hampers cognitive ability. Neurobiological stress reactions, for example HPA axis reactivity and the release of stress hormones, can have lasting negative effects on cognitive functions [220]. A reciprocal effect that lowers cognitive ability and emotional control over time might contribute in strengthening their association. If so, it is possible that interventions to compensate for poor cognitive ability and emotional control early in life would reduce this adverse effect.

Social problems or maladjustment during upbringing, indicated here by contact with police or child care authorities, might be seen in several ways. One is that lower problem-solving abilities or other intelligence-related factors in the individual or among others in the close environment might increase the risk for such problems (since intelligence is highly heritable, intelligence level in the individual is correlated with the intelligence level of the biological family). This mechanism has been suggested to partly explain the higher risk in men with lower intelligence for being convicted for violent crimes [221] or being a victim of homicide [222,223].

Another view is that such problems might indicate problematic circumstances in childhood or adolescence, which might also have an adverse effect on neuro-physiological systems, increasing stress reactivity as explained above. Childhood socioeconomic position or crowded housing did not contribute in the associations between intelligence and any health outcomes in our studies, but it is possible that those variables did not capture the psychosocial environment during upbringing. Adverse circumstances and stress in childhood can have a negative impact on cognitive and emotional functioning [101], and morbidity and mortality [140,141,224,225]. The substantial prevalence of child maltreatment in general, high-income populations [226] suggests that such circumstances might have an impact on a public health level. Adverse events might of course have an impact on several of the variables in the studies, including the personality aspects, psychiatric disorders, substance use, and later

morbidity and mortality. However, this mechanism is speculative; but one study did find that family social circumstances contributed to the negative association of intelligence with adverse outcomes such as substance abuse, suicide attempt and unemployment in a cohort of young people in New Zealand [68].

It is noteworthy that some aspects of intelligence have been found to be positively associated with some expressions of psychological distress, mainly in younger samples. For example, higher intelligence in childhood was associated with a higher risk for self-harm in adolescence in a cohort of British girls and boys followed up to age 17 [69]; and higher verbal intelligence was associated with worry and rumination in a sample of 126 undergraduate students with a mean age of 20 years [227]. It is possible that the relation between intelligence and psychological distress differs between groups based on, for example, age or sex.

Health behaviours are suggested to have a mediating role in the association between intelligence and health [1,132], and we did find that smoking, risky use of alcohol and BMI at conscription contributed substantially to the association of intelligence with mortality among men with CHD (but not as much in the association with disability pension). However, health behaviours might also act as confounders in associations of intelligence with somatic and psychiatric health, since some health behaviours, for example exercise, weight gain, and alcohol use, are suggested to affect not only health but also cognitive ability [116,118,228,229,230]. On the other hand, considering the relatively modest effect of environmental factors on intelligence [87], the role of health behaviours as confounders in the association of early-life intelligence with morbidity and mortality might be limited at the population level.

In a life course perspective, it is possible that intelligence, and other individual factors such as personality, lay the ground for an accumulation of factors and circumstances over the life course, that might be cumulatively good or bad for health [231]. Suppose a person is born with relatively low intelligence, high neuroticism and low agreeableness – that person will have to struggle a lot harder to attain the same good foundation for a healthy and long life as a person born with higher intelligence, lower neuroticism and higher agreeableness. They will probably have different possibilities and hindrances in their environments – in school, with peers and authorities, and so on – and the basic innate differences will turn into differences in life styles, in socioeconomic and social circumstances. Given that such traits are heritable [232], chances are that the latter person is also born into a more beneficial psychosocial environment than the former, further increasing the disproportion in conditions. Some of the differences in conditions might then be passed on to the next generation: studies have found that parent's IQ is associated with the risk for injuries in their children [102], children's sedentary behaviour [103], and smoking during pregnancy [233].

It is of course also possible that an accumulative association between intelligence and health risks is independent from other traits, operating entirely through education and socioeconomic and social circumstances in adulthood. Higher intelligence is indeed associated with upward social mobility [234], also when emotional functioning is taken into account [180]. Furthermore, since cognitive change across the life course is in itself affected by factors that are often predicted by intelligence, such as education

[110] and intellectual leisure activities [235], or the health behaviours mentioned above, cognitive change can also be seen as a part of the accumulation model.

Other psychological factors might also contribute to a clustering of intelligence and other health-affecting traits. In a study of 606 US men and women, preference for immediate rewards was associated with general intelligence, controlling for demographics, education, income and impulsiveness [236]. Interpersonal skills might also be better with higher intelligence [237]. On the other hand, competencies and skills that might be easier to affect than intelligence might compensate for lower intelligence. For example, studies found that people with low IQ but high emotional intelligence got as good ratings on job performance [238] and effective self-presentation [239] as people with high IQ.

5.4 METHODOLOGICAL CONSIDERATIONS

5.4.1 Strengths

The main strengths of these studies are the large and representative samples of a general male population, and the ample data collected at conscription and obtained through record linkage with various national records. Since conscription was mandatory by law, there is no self-selection. The exposure variable, intelligence, was measured using a standardised battery, developed for assessing general ability. The outcomes in the longitudinal studies are based on national records with high reliability, with near complete follow-up from early adulthood up to age 59.

5.4.2 Limitations

The downside of using conscription data is that no women were obliged to participate, so the data do not include women. Associations of intelligence with for example suicide might differ between women and men [40]. Furthermore, the cohort comprises primarily Swedish-born men in a homogenous age group. Interpretations of the results and generalisations to other populations should be done with these limitations in mind. In addition, men with documented chronic illness or disability were exempted from conscription and are not included in the cohort.

It can be argued that intelligence measured at age 18-20 might be affected by education, injuries and other environmental factors during the first two decades of life, and that intelligence measured in childhood would be more pure. However, due to differences in cognitive maturity rate, intelligence measured in children might not be fully representative for the individual across time. There are individual differences in how intelligence develops in children [240], and those with higher potential might even develop at a slower rate than others [241]. Therefore, intelligence measured in late adolescence or young adulthood may in some ways be more reliable; so studies with intelligence measured at different ages can be said to complement each other. Furthermore, intelligence was measured at only one point in time, and might not be fully representative of cognitive ability during the entire follow-up. Intelligence is quite stable over time, but not perfectly [76,77].

Information on lifestyle variables at conscription (smoking, risky use of alcohol, and BMI) was used as measures of individual lifestyle risk factors in studies II and IV. These factors have previously been found to predict CVD and mortality in this cohort [242,243]. However, if these variables are seen as indicators of long-term health behaviours over the life course, using a measure in early adulthood might introduce misclassification since health behaviours can change over time. Socioeconomic circumstances and family formation in adulthood were also obtained at one point in time (although the time point for civil status in study IV varied between individuals), and are likely to change over time. Assuming that higher intelligence is not associated with a higher relative increase (or less decrease) in the prevalence risk factors over time, that is, that the misclassification is non-differential or differential in favour of those with higher intelligence, the effects of these factors are most likely to be underestimated in the statistical models. Previous studies have shown that quitting smoking was unrelated to intelligence in a subsample of men with self-reported data on smoking at age 30 to 53 in this cohort [25], and that lower intelligence was associated with greater weight gain in adulthood in other cohorts [133,134,174]. A differential misclassification that would overestimate the effect of these factors is unlikely. Moreover, the use of several overlapping indicators for socioeconomic position, health behaviours or personality aspects reduces the risk that misclassification would cause an underestimation of their explanatory effect [244].

It is possible that the information the conscripts reported in the questionnaires about events earlier in their life, such as contact with police and child care authorities, or the information reported in the interview with the psychologist that made the basis for the personality assessment, was biased due to the retrospective nature of the data collection. Thus, the effect of those factors in the association between intelligence and health outcomes might be underestimated, and thereby also their impact as explanatory covariates in the statistical analyses. It is also possible that the information the psychologist obtained about the conscript, or traits such as verbal ability during the interview, biased their evaluation of emotional control and social maturity. Responses related to higher intelligence might have created a “halo effect”, a bias towards a more positive evaluation, which might contribute to correlations between intelligence, emotional intelligence and social maturity. If so, the contribution of the personality variables on the association between intelligence and the outcomes would be overestimated. However, there was a fairly high correlation ($r=.85$) between psychologists ratings in inter-rater testing using tape-recorded interviews [186].

Information on suicide attempt and death by suicide, used as outcomes in study I, were obtained from the national hospital discharge register and cause of death register, respectively. This means that those men who did not receive hospital care or did not stay overnight after an attempt, were not included in our analyses. It is possible that the association between intelligence and suicide attempt is different among those who are never recorded in hospital registers after an attempt. It also means that the diagnosis of suicidal intent is dependent on the judgment of the doctor or coroner. The inclusion of undetermined intent reduces the risk of underestimation of cases. Most deaths with undetermined intent are likely to be suicides [199,200]. Information on CHD, used in study IV, was also obtained from the patient register, and it is possible that some events

were silent and not registered. However, the analysis restricted to MI, a severe event which is less likely to be neglected, yielded similar results. Diagnoses prior to, or co-occurring with, the first CHD diagnosis, was also obtained from the patient register. Those who were not treated in inpatient care were not registered and comorbidity was therefore likely to be underestimated. If this underestimation differed between levels of intelligence, it might over- or underestimate the effect on the association between intelligence and the outcomes. However, it is unlikely that any such over- or underestimation would have affected the interpretation of the main results.

5.4.3 Covariates: confounders, mediators, or both?

Traditionally in epidemiology, one aims to adjust for confounding factors in analyses of exposures and outcomes. However, in cognitive epidemiology, as well as in life course epidemiology, it is common to adjust also for factors assumed to lie on the path between the exposure (intelligence) and the outcome (most often morbidity or mortality) [5]. This is done in order to investigate possible mediators in the associations, while there is perhaps less interest in finding a “true” effect of intelligence on the various outcomes, but rather to understand the mechanisms in order to find efficacious interventions.

Nevertheless, when intelligence measured early in life is regressed onto morbidity and mortality much later in life, it is fair to assume that intelligence leads to the disease and not the other way around, that the disease would be present already in youth and affect cognitive ability. When we make this assumption, it would be a case of reverse causality if the disease, or a precursor of the disease, really was present and had this adverse effect. As time of measurement to follow-up increases, the risk for reverse causality decreases. In the longitudinal studies (I, II and IV), analyses are performed with a follow-up time in middle age up to age 57 or 59 which minimizes the risk for reverse causality. Moreover, adjusting for diagnoses in youth had no or moderate attenuating effect on the associations. We also saw in study III that somatic health in youth was not very strongly associated with intelligence in comparison with the associations of intelligence and health outcomes later in life. However, in study III, which is cross-sectional by design, any assumptions of the direction of the associations come with a greater risk for reverse causality, which is why we have to be careful in making such assumptions (see section 6.3 for examples of interpretations of the association).

Furthermore, for some of the covariates that contribute to the association we cannot be sure of the causality either. Since intelligence is quite stable across life [76,77], it is possible that an individual’s intelligence level affects other variables even if intelligence is measured at the same time, or even later. In our studies, it is hypothetically possible that the conscripts’ intelligence level affected their history of smoking and alcohol use, for example. Similarly, other factors might have affected intelligence or IQ regardless of when they are measured, such as education. In addition, they might affect each other in a mutual process; or they might both be affected by a third variable which would make the covariate a mere proxy.

Education is often mentioned as a variable to be careful with since it can be viewed as a proxy for intelligence, and adjusting for education might be considered an over-adjustment [29,129]. Education is included in the model investigating the association of intelligence with disability pension (study II) since it was considered an important possible contributing factor in the association. In this context, education is regarded as having a primarily mediating role in the association, but its role as a confounder or a proxy for intelligence is difficult to disentangle.

Height is used as an indicator of socioeconomic circumstances in studies I and III, as is common in life course studies [181]. However, it is possible that height is related to intelligence in other ways. Possible mechanisms, besides common environmental factors, include pleiotropic genes (genes that affect more than one manifested trait), and assortative mating (intelligent and tall people tend to have children with intelligent and tall partners) [245,246]. Thus, when including height in the models, it is possible that we also adjust for a shared genetic component. However, including height had generally minimal or no effect on the association between intelligence and the outcomes. The one exception is physical fitness in study III for which height attenuated its association with intelligence. In this context, we cannot rule out the possibility that shorter stature was a disadvantage in the cycling test that measured physical fitness.

The choice of analytic methods, logistic regression and survival analysis, is partly related to the tradition in life course studies and the intention to make the results easy to compare with previous findings. Partly, it is because causality between intelligence and the covariates is not known. Structural equation modeling (SEM), which might otherwise be appropriate for investigating associations and contributing variables, requires stronger assumptions about causality and interaction between variables [247] which makes it inappropriate in our analyses.

5.5 FINAL REMARKS AND FUTURE DIRECTIONS

The idea that intelligence is associated with health outcomes across the life span might be surprising to some, and perhaps even discouraging. In public health, there is an aim to mitigate inequalities in health; but how can the society deal with health inequalities connected to a strongly heritable, individual trait? Perhaps it is even difficult to believe that such differences exist – maybe not so much because it seems unbelievable, at least not when given some thought, but because it seems difficult to do anything about - and perhaps also very unfair.

Another way to react it is to say that disadvantages related to intelligence level are not really inequalities that should be counteracted. Some might say that differences in ability and performance are fair bases for differences in outcomes such as well-being or health. Some might say that while socioeconomic inequalities in health are unwanted as long as it occurs at a structural level, there is not much to do about individuals who fail to attain a high socioeconomic position in a democratic society (or worse, who do not even try) or use less healthy ways of coping with their everyday life.

To that, Mackenbach has an answer: “Old forms of disadvantage seem to have been replaced partly by new forms, disguised as personal characteristics such as personality and cognitive ability. Premature deaths in populations with low socioeconomic status

that are linked to certain personality profiles or cognitive abilities, which in turn are related to genetic factors, early environment, social mobility, or a combination of these, are no less unfair than are premature deaths attributable to poverty, unsafe working conditions, or absence of health care.” [248, p. 854-855].

This work is conducted in accordance with this notion, and with the belief that in order to reduce the inequalities, we need to know about the mechanisms that underlie them. This thesis contributes with a few pieces of this puzzle, but much still remains to be investigated.

First, these studies included only men. Since many of the studies on intelligence and health also are based on male populations, including the largest ones, more studies on the associations among women are needed. Furthermore, since associations of intelligence with psychiatric and somatic health outcomes seem to differ between age groups, a clearer picture of the associations across the life course would also be informative. For example, we found that some aspects of somatic health were associated with intelligence in a cross-sectional analysis in youth. Investigating the role of early somatic morbidity for morbidity later in life would be informative.

The inverse association intelligence with psychiatric disorders with was stronger than the association with other diagnoses and health indicators, and associations between intelligence and psychiatric illness has been found several in other studies [12,21,59,60,61,62,63]. The role of psychiatric illness and other aspects of low mental well-being in the associations of intelligence with morbidity and mortality should be further studied.

Following from the reasoning in section 5.4.3, causality between intelligence and the factors contributing to the associations with the outcomes is difficult to determine in the studies in this thesis, not least regarding the variables that are measured at the same time as intelligence. Nevertheless, one way to interpret the results in life course terms is that the findings are compatible with an accumulation of risk model, with various factors contributing over the life course to the association of early life intelligence with morbidity and mortality. A task for future studies is to determine the directions of the associations between intelligence and such contributing factors, or possible underlying causes, in order to identify efficient interventions.

In the fully adjusted models, intelligence was still associated with suicide, suicide attempt, and disability pension, and there was a remaining tendency of associations with mortality in the sample of men with CHD. To what extent such remaining associations are accounted for by system integrity, everyday life management or other factors that were not included in our models is also left to future research.

5.6 CONCLUSIONS

In line with previous findings, we found that intelligence in early adulthood was inversely associated with suicide, suicide attempt and disability pension in men (study I and II). Here, the follow-up periods were extended up to age 57 (suicide and suicide attempt) and 59 (disability pension), showing that the associations remain through middle age. The associations were graded across the range of intelligence.

In the associations of lower intelligence with suicide and suicide attempt, adjustment for psychiatric diagnosis, social problems and aspects of personality in young adulthood, and social circumstances in later adulthood, attenuated the associations. Thus, these were factors that contributed to the observed associations. Childhood socioeconomic position had no impact on the associations. Although attenuated, the larger part of the associations remained after adjustment.

In the association of lower intelligence with disability pension, adjustment for psychiatric diagnosis, aspects of personality and health lifestyle factors in youth had some attenuating impact, while socioeconomic and work-related factors in adulthood, after labour market entry, attenuated the associations more. Childhood socioeconomic position had no impact on the associations. Also here, a considerable part of the association remained after adjustment.

Lower intelligence was associated with a higher risk for several of the ICD-8 diagnoses and all other indicators of poor health that were assessed at conscription, in cross-sectional analyses (study III). This included, for example, endocrine disorders, diseases of the ear, digestive system disorders and self-rated health. However, the risk was decreased for a few of the diagnoses, including hayfever and diseases of the eye. The strongest association was with psychiatric diagnoses, but psychiatric comorbidity did not explain the associations of intelligence with the other diagnoses and health indicators. Childhood socioeconomic position had no or minimal impact on the associations.

Among men with CHD in middle age, intelligence in youth was not associated with the risk for recurrence (study IV). By contrast, lower intelligence was associated with higher case-fatality rate at the first event and higher mortality during 17 years of follow-up. These associations were attenuated after adjustment for individual factors measured in youth, and socioeconomic and social factors in adulthood. Childhood socioeconomic position had no impact on the associations.

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